IPA 系統生物學分析軟體暨資料庫教育訓練

IPA以數據演算及人工閱讀的資料庫文獻，
提供您快速的在數千萬筆的研究分析資料中，
找到最關鍵的生物途徑與分子間調控關係。

高雄醫學大學 KAOHSIUNG MEDICAL UNIVERSITY 1954

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Ingenuity **Pathway** Analysis

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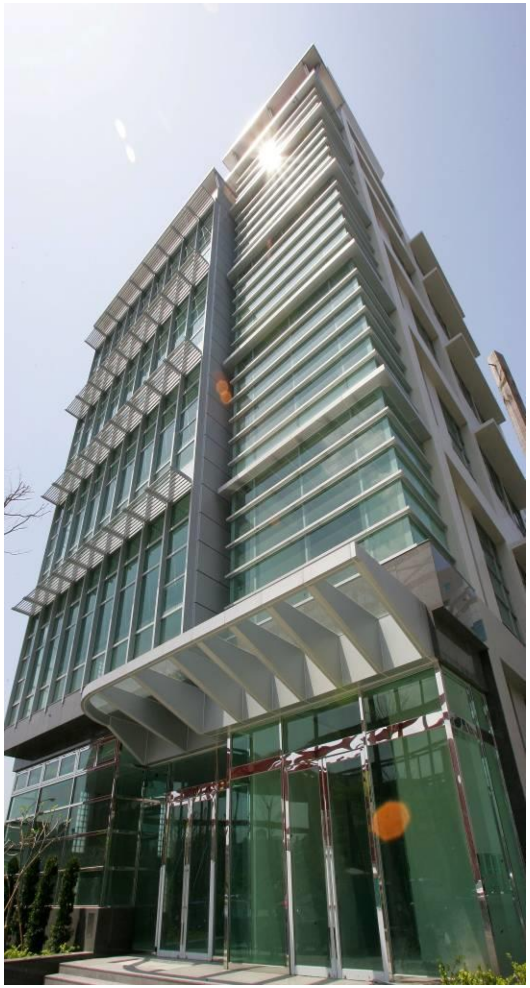
About GGA



GGA is part of the BIONET Group (訊聯生物科技)

CEO: Christopher Tsai, Ph.D. 蔡政憲 博士

Established: Nov. 2008

Main Product & Service Areas:

- Genetic Testing & Molecular Diagnosis
- **Scientific Informatics & Bio IT**

IPO Date: September 17, 2012

Stock Ticker: 4160 (Taiwan OTC)

Molecular Science Center in GGA

在地化服務
使用者教育訓練

生物資訊

世界一流
資訊產品
軟體與資料庫

企業品質
管理系統

化學資訊

*** FIRST ***

分子視算中心
MSC

*** ONLY ***

電子化
實驗室管理

生命科學

合規電腦
系統確效(CSV)

奈米與
材料科學

安裝與調校

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IPA

IPA orthologous :

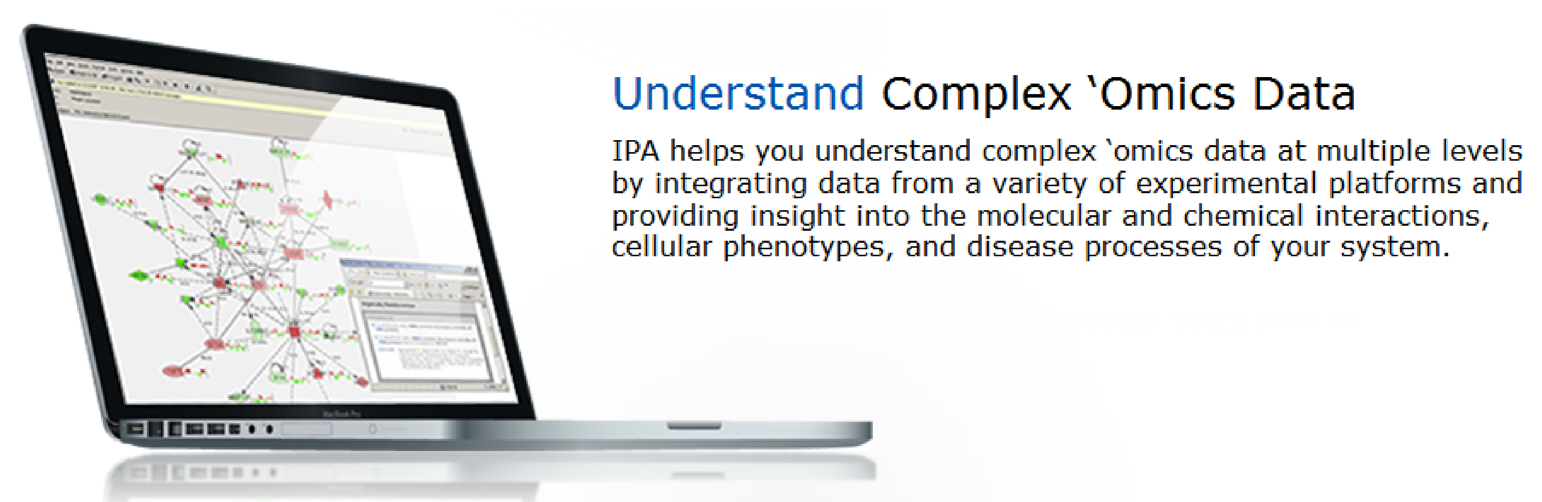
Arabidopsis thaliana
Bos taurus (bovine)
Caenorhabditis elegans
Gallus gallus (chicken)
Pan troglodytes (chimpanzee)
Danio rerio (zebrafish)
Canis lupus familiaris (canine)
Drosophila melanogaster
Macaca mulatta (Rhesus Monkey)
Saccharomyces cerevisiae
Schizosaccharomyces pombe

IPA supported platform :

- **Gene expression:**
  - qPCR analysis
  - Microarray
  - RNA-Seq (NGS)
  - microRNA
  - mRNA
- **Proteomics**
  - PhosphoProteomics New
- metabolomics

IPA application:

- Biomarker finding
- Toxicity Functions
- Diseases regulation



Understand Complex ‘Omics Data

IPA helps you understand complex ‘omics data at multiple levels by integrating data from a variety of experimental platforms and providing insight into the molecular and chemical interactions, cellular phenotypes, and disease processes of your system.

Supported Identifiers for Data Upload

Get more complete mapping during dataset upload!

Vendor IDs	Gene	Protein	Transcript	microRNA	SNP	Chemical
Affymetrix (na36)	Entrez Gene (2020/10)	GenPept	Ensembl (101)	miRBase (mature)	Affy SNP IDs	CAS Registry Number
Agilent	GenBank (239)	International Protein Index (IPI)	RefSeq (human、mouse)	miRBase (stemloop)	dbSNP	HMDB
Life Tech (ABI)	Symbol-human (HUGO/ HGNC, EG)	UniProt/ Swiss-Prot Accession (2020_03)	UCSC (hg18)			KEGG
Codelink	Symbol- mouse (EG)		UCSC (hg19)			PubChem CID
Illumina	Symbol- rat (EG)		UCSC (hg38)			
Ingenuity	GI Number					
	UniGene					

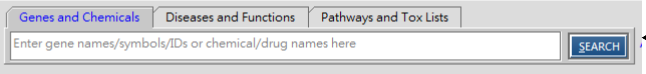
Entry Points in IPA

Biological Questions

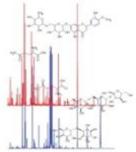
Search

Experiment Data

Custom Pathway

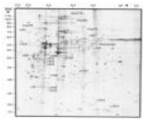


Expression arrays

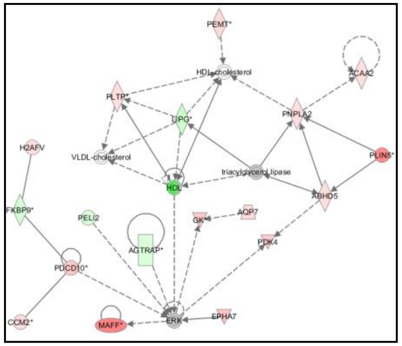


Mass spec

Protein arrays



2D Gel electrophoresis

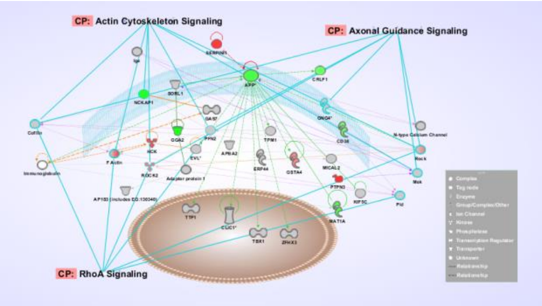


Networks

Bio/Tox Functions
Diseases/Disorders
Canonical Pathways
Upstream regulators
Mechanistic/Casual Network
Interaction Network

Core **IPA-Biomarker**

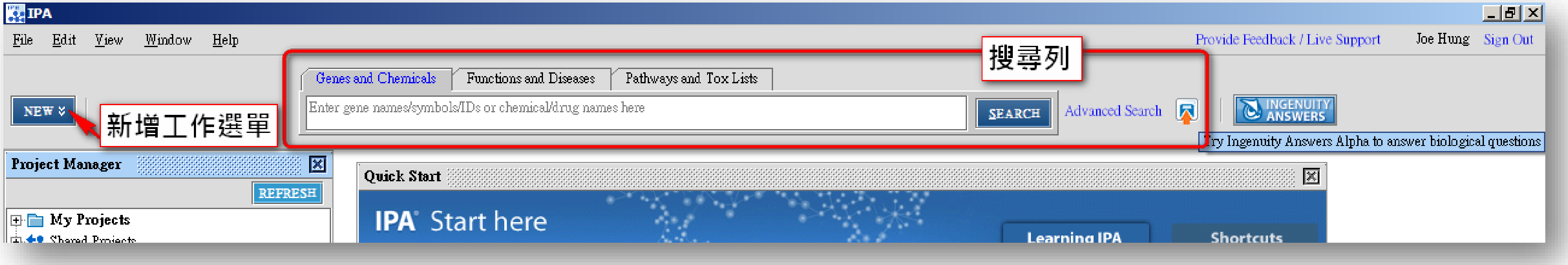
IPA-Tox **IPA-Metabolomics**



Communicate & Collaborate

Searching

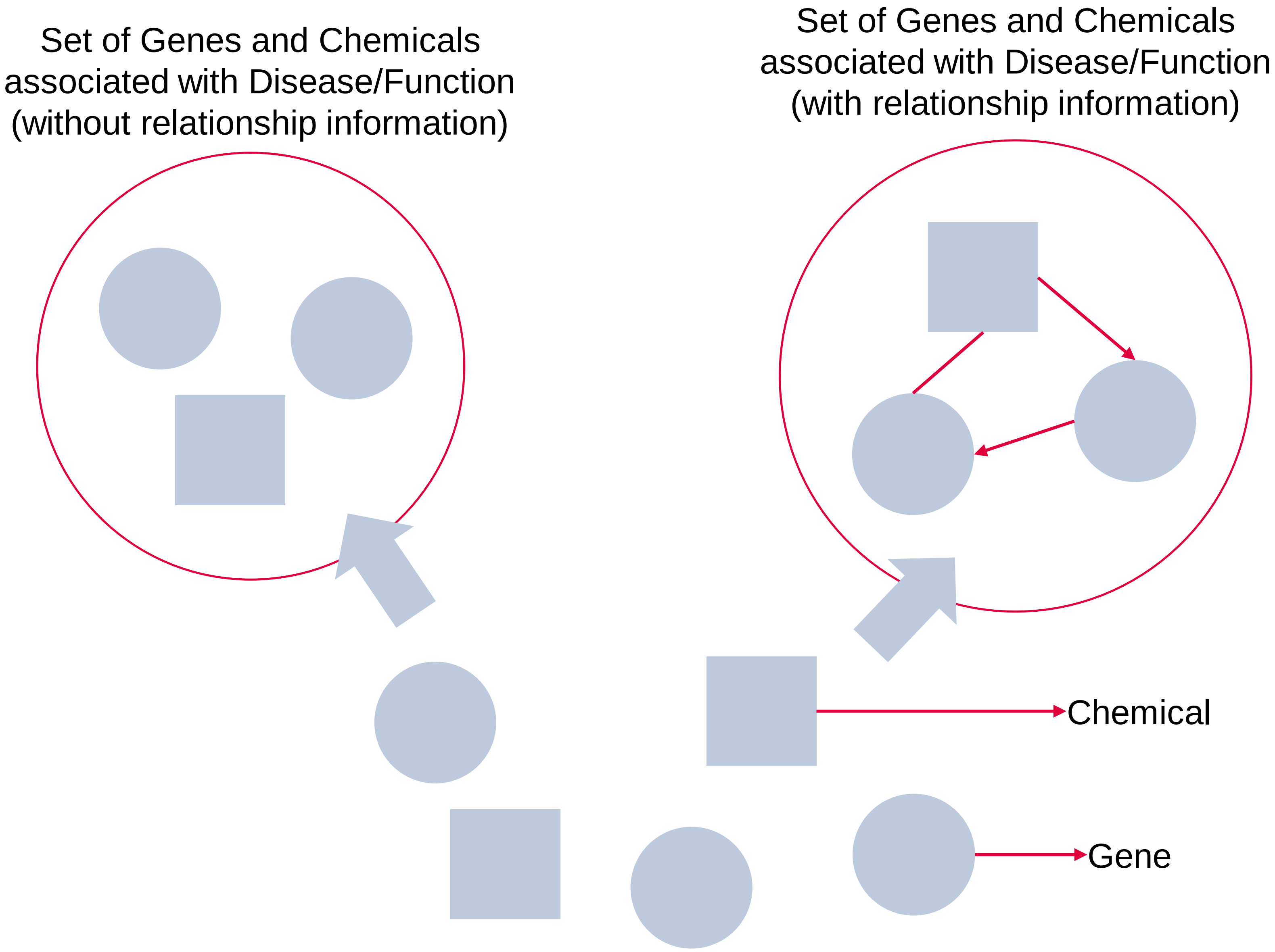
- **Genes and chemicals**
- **Diseases and Functions**
- **Pathways and tox lists**
- Advanced search: Limiting results to a molecule type, family or subcellular location



Enter gene names/symbols/IDs or chemical/drug names here

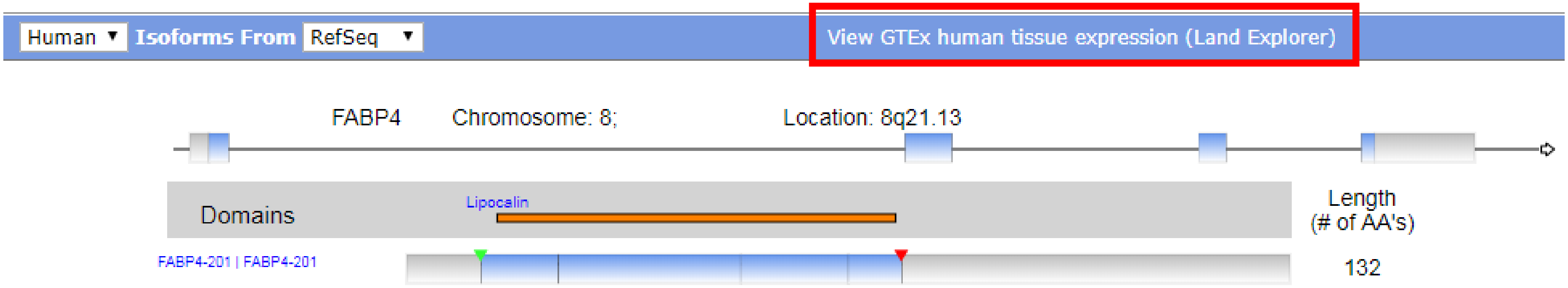
Try Ingenuity Answers Alpha to answer biological questions

Scales for Gene/Chemical, Disease, Pathway



Gene View

- **Explore sample-level human tissue expression through OmicSoft Land Explorer**



Now you can examine detailed expression patterns across human tissues directly from IPA's Isoform Views. IPA now offers access to a lite version of OmicSoft Land Explorer. With this new feature, you can provide interactive plots of gene expression in 51 different human tissues from the GTEx project, for both gene level and individual splice variants. You can filter the view for a particular tissue, or filter on metadata, such as tissue donor age or gender. You can also download the detailed sample-level expression data for the gene.

Key Terminology

- **Finding:6.6 million**
  - A single piece of evidence from a literature source or database in the **Ingenuity Knowledge Base**
  - Includes context of the fact such as experiment type, species, tissue/cell location, etc.

- **Canonical Pathway (Signaling and Metabolic)**
  - Are generated prior to data input, based on the literature
  - Do NOT change upon data input
  - Do have directionality

Basic Module and Advanced module on IPA

Basic Module

- Gene and Chem View
- Isoform View
- Disease View
- Canonical Pathway
- BioProfiler
- Upload Dataset
- Molecule Activity Predictor (MAP)
- Tox Lists and Tox Functions
- Interactive Disease and Functions Nodes
- Biomarker filter
- Path Designer

https://www.qiagenbioinformatics.com/products/features/

Advanced Analytics (AA)

- Causal Network Analysis
- Upstream regulator Analysis
- Downstream Effects Analysis
- Regulator Effects
- Network Analysis
- Mechanistic Network
- Activity Plot
- Graphic Summary
- Analysis Match

- MicroRNA Target Filter
- Relationship Export
- IsoProfiler
- Comparison Analysis
- PhosphoProteomics Analysis

https://www.qiagenbioinformatics.com/files/flyers/IPA_Advanced_Analytics_WEB.pdf

Live Demo

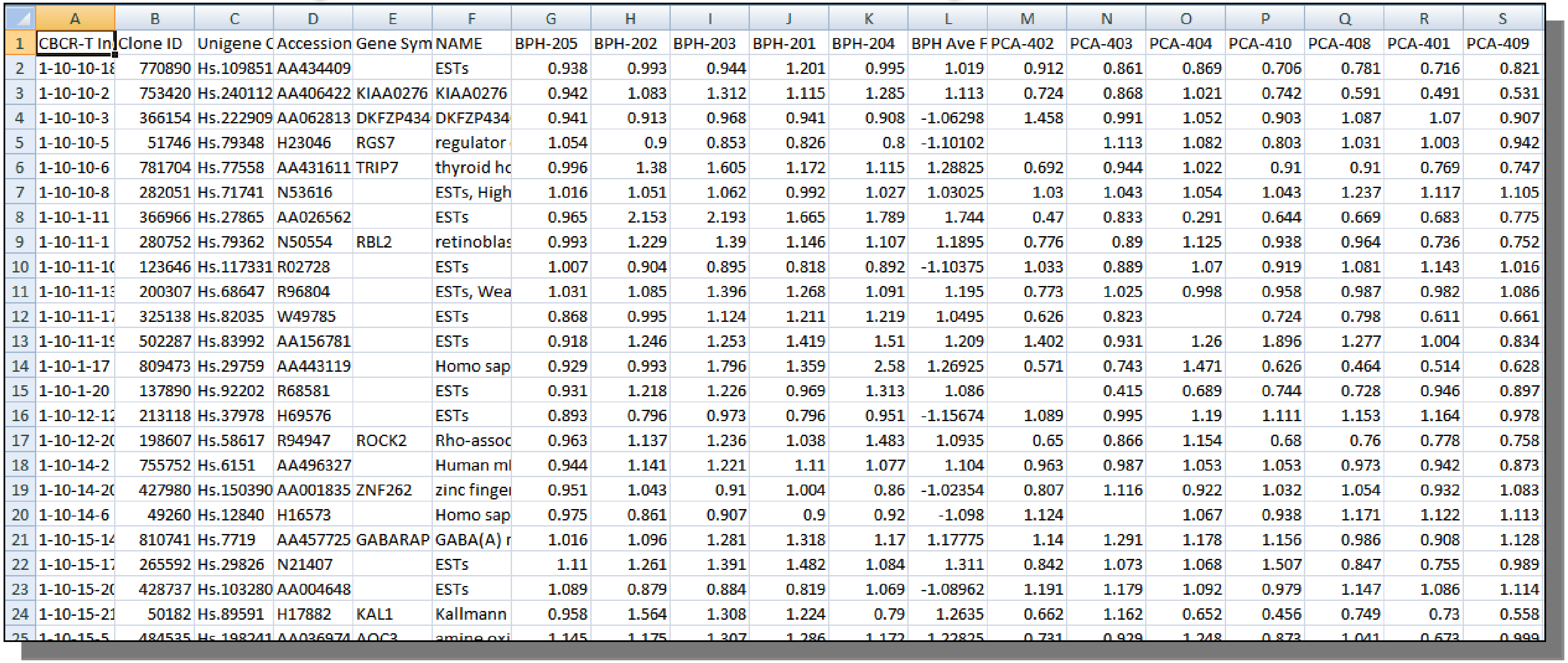
準備IPA分析用的Dataset

必須有一欄放入ID

Replicates

Average

Other observations (Comparison)



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	CBCR-T In	Clone ID	Unigene C	Accession	Gene Sym	NAME	BPH-205	BPH-202	BPH-203	BPH-201	BPH-204	BPH Ave F	PCA-402	PCA-403	PCA-404	PCA-410	PCA-408	PCA-401	PCA-409
2	1-10-10-18	770890	Hs.109851	AA434409		ESTs	0.938	0.993	0.944	1.201	0.995	1.019	0.912	0.861	0.869	0.706	0.781	0.716	0.821
3	1-10-10-2	753420	Hs.240112	AA406422	KIAA0276	KIAA0276	0.942	1.083	1.312	1.115	1.285	1.113	0.724	0.868	1.021	0.742	0.591	0.491	0.531
4	1-10-10-3	366154	Hs.222909	AA062813	DKFZP434	DKFZP434	0.941	0.913	0.968	0.941	0.908	-1.06298	1.458	0.991	1.052	0.903	1.087	1.07	0.907
5	1-10-10-5	51746	Hs.79348	H23046	RGS7	regulator	1.054	0.9	0.853	0.826	0.8	-1.10102		1.113	1.082	0.803	1.031	1.003	0.942
6	1-10-10-6	781704	Hs.77558	AA431611	TRIP7	thyroid hc	0.996	1.38	1.605	1.172	1.115	1.28825	0.692	0.944	1.022	0.91	0.91	0.769	0.747
7	1-10-10-8	282051	Hs.71741	N53616		ESTs, High	1.016	1.051	1.062	0.992	1.027	1.03025	1.03	1.043	1.054	1.043	1.237	1.117	1.105
8	1-10-1-11	366966	Hs.27865	AA026562		ESTs	0.965	2.153	2.193	1.665	1.789	1.744	0.47	0.833	0.291	0.644	0.669	0.683	0.775
9	1-10-11-1	280752	Hs.79362	N50554	RBL2	retinoblas	0.993	1.229	1.39	1.146	1.107	1.1895	0.776	0.89	1.125	0.938	0.964	0.736	0.752
10	1-10-11-10	123646	Hs.117331	R02728		ESTs	1.007	0.904	0.895	0.818	0.892	-1.10375	1.033	0.889	1.07	0.919	1.081	1.143	1.016
11	1-10-11-13	200307	Hs.68647	R96804		ESTs, Wea	1.031	1.085	1.396	1.268	1.091	1.195	0.773	1.025	0.998	0.958	0.987	0.982	1.086
12	1-10-11-17	325138	Hs.82035	W49785		ESTs	0.868	0.995	1.124	1.211	1.219	1.0495	0.626	0.823		0.724	0.798	0.611	0.661
13	1-10-11-19	502287	Hs.83992	AA156781		ESTs	0.918	1.246	1.253	1.419	1.51	1.209	1.402	0.931	1.26	1.896	1.277	1.004	0.834
14	1-10-1-17	809473	Hs.29759	AA443119		Homo sap	0.929	0.993	1.796	1.359	2.58	1.26925	0.571	0.743	1.471	0.626	0.464	0.514	0.628
15	1-10-1-20	137890	Hs.92202	R68581		ESTs	0.931	1.218	1.226	0.969	1.313	1.086		0.415	0.689	0.744	0.728	0.946	0.897
16	1-10-12-12	213118	Hs.37978	H69576		ESTs	0.893	0.796	0.973	0.796	0.951	-1.15674	1.089	0.995	1.19	1.111	1.153	1.164	0.978
17	1-10-12-20	198607	Hs.58617	R94947	ROCK2	Rho-assoc	0.963	1.137	1.236	1.038	1.483	1.0935	0.65	0.866	1.154	0.68	0.76	0.778	0.758
18	1-10-14-2	755752	Hs.6151	AA496327		Human ml	0.944	1.141	1.221	1.11	1.077	1.104	0.963	0.987	1.053	1.053	0.973	0.942	0.873
19	1-10-14-20	427980	Hs.150390	AA001835	ZNF262	zinc finger	0.951	1.043	0.91	1.004	0.86	-1.02354	0.807	1.116	0.922	1.032	1.054	0.932	1.083
20	1-10-14-6	49260	Hs.12840	H16573		Homo sap	0.975	0.861	0.907	0.9	0.92	-1.098	1.124		1.067	0.938	1.171	1.122	1.113
21	1-10-15-14	810741	Hs.7719	AA457725	GABARAP	GABA(A) r	1.016	1.096	1.281	1.318	1.17	1.17775	1.14	1.291	1.178	1.156	0.986	0.908	1.128
22	1-10-15-17	265592	Hs.29826	N21407		ESTs	1.11	1.261	1.391	1.482	1.084	1.311	0.842	1.073	1.068	1.507	0.847	0.755	0.989
23	1-10-15-20	428737	Hs.103280	AA004648		ESTs	1.089	0.879	0.884	0.819	1.069	-1.08962	1.191	1.179	1.092	0.979	1.147	1.086	1.114
24	1-10-15-21	50182	Hs.89591	H17882	KAL1	Kallmann	0.958	1.564	1.308	1.224	0.79	1.2635	0.662	1.162	0.652	0.456	0.749	0.73	0.558
25	1-10-15-5	484535	Hs.198241	AA036974	AOC3	amine oxi	1.145	1.175	1.307	1.286	1.172	1.22825	0.731	0.929	1.248	0.873	1.041	0.673	0.999

準備IPA分析用的Dataset

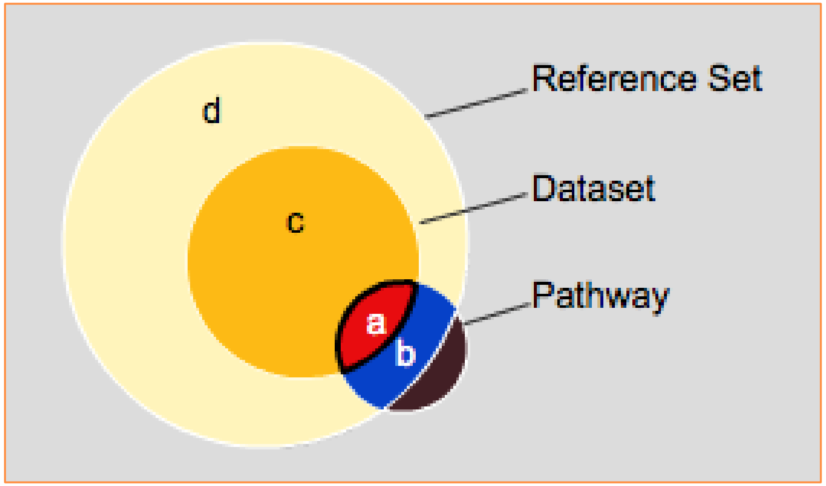
- 重複性實驗的數值平均、p-vlaue或fold-change等統計計算，要先在IPA分析之前完成。

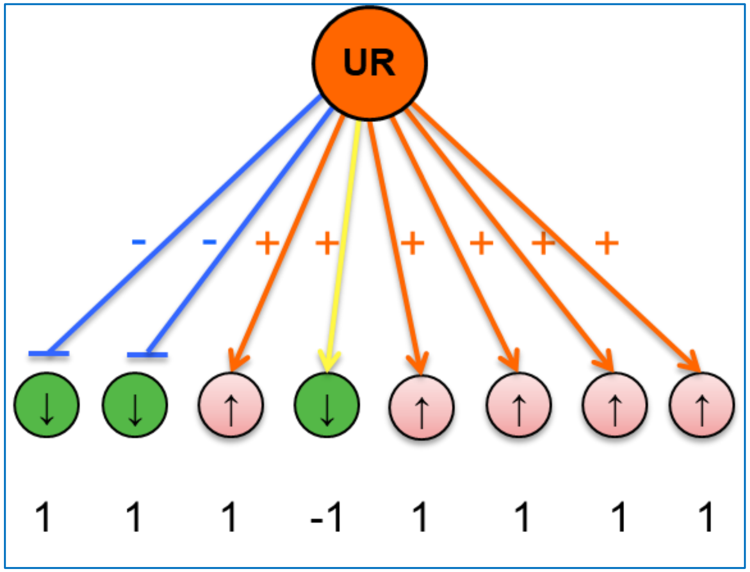
- 將實驗資料用 Excel 表格檔案儲存，檔案裡面只能有一個Sheet存在。
  - □ Excel Sheet當中必須要有一欄是列出**分子的ID** (如Gene Symbol, Refseq number, Uniprot number, HMDB等常用命名皆支援)
  - □ 每個Excel Sheet 最多可以放入 **20個 observations** (即20個實驗變因的資料欄的意思)
  - □ 每個Observation可以有3個不同的表現值種類 (ex. p-Value，fold-change等)
  - □ **表格欄位最上方只能有一個Head row (首行)**
  - □ 資料上傳到IPA後，可以在cut-off 值欄位進行設定，讓使用者決定門檻來決定**表現顯著有差異**的生物分子。意味著原始實驗資料中有些分子的數值不夠顯著，可以用cut-off值作為門檻排除於分析運算中。那些通過cut-off值的分子們在IPA中稱之為Analysis-Ready Molecules。

Statistical Analysis Used in IPA

P-value of overlap

- Null hypothesis: No overlap between molecule from dataset and disease/function/upstream regulator/pathway.
- Calculate using the right-tailed Fisher's Exact Test
- Significant p-value ≦ 0.05



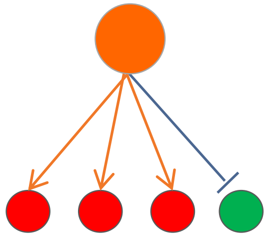


Z-score

- Predicts Activation or Inhibition
- Correlation between what is known (IPA Knowledge Base) and your expression data

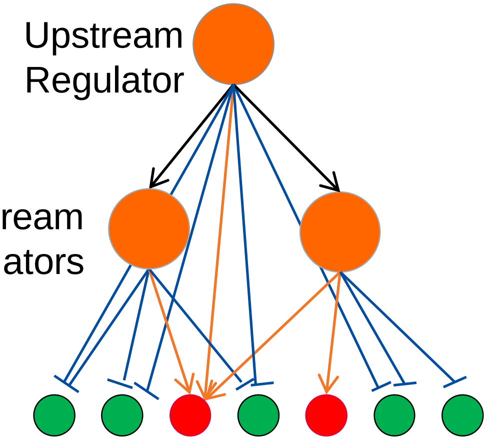
Network types in IPA

Upstream Analysis



Dataset Molecules

Mechanistic Network of Upstream Regulators



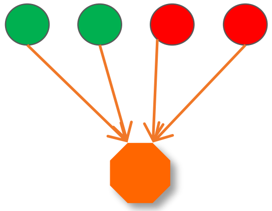
Upstream Regulator

Other upstream regulators

Dataset Molecules

Function Analysis

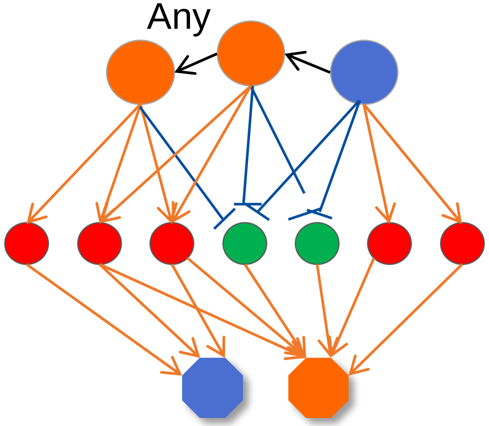
Dataset Molecules



Diseases / functions

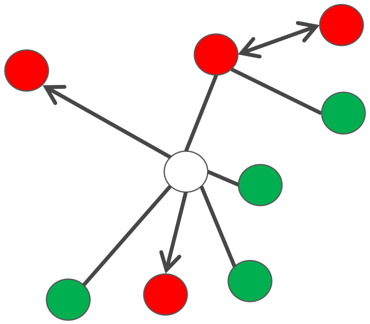
Regulator Effect Network

Any



Diseases / functions

Interaction Network



Dataset Molecules

IPA 分析結果

Summary: 將顯示前五名各頁籤之分析結果

Graphical Summary: 總和各生物主題之分析結果(路徑、上游調控、疾病)

Canonical Pathways : 列出受實驗影響的Signaling Pathway與Metabolic Pathway

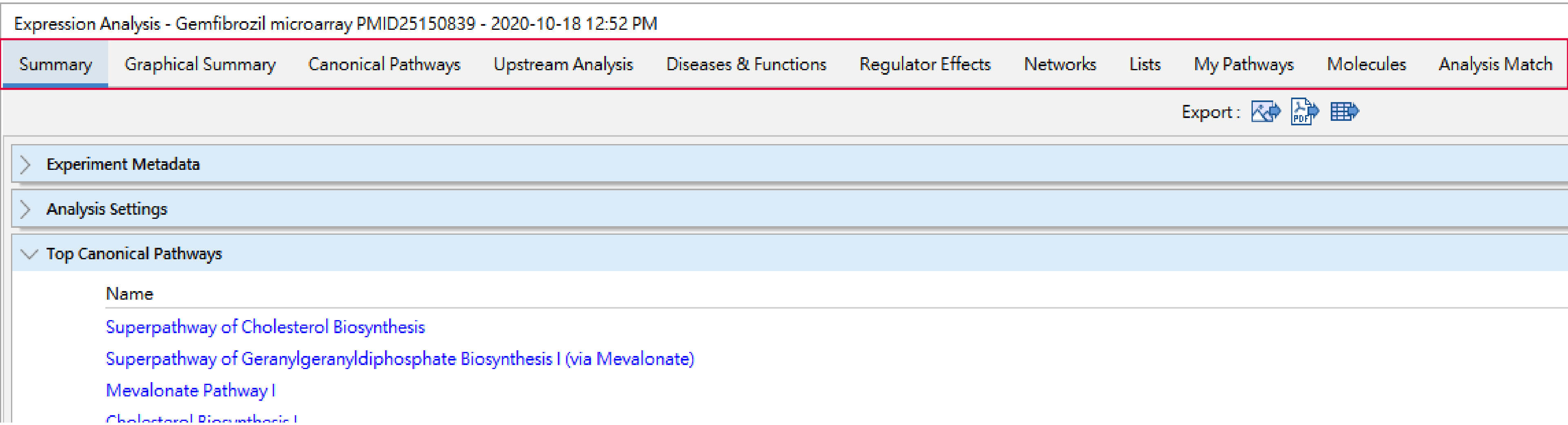
Upstream Analysis: 列出與資料中變動分子有關的Upstream molecules，以及根據研究文獻預測它們是否是被啟動或是被抑制。

Disease&Function : 了解實驗結果在各分析疾病調控上之結果

Networks : 呈現實驗資料中的分子間的網路關係 。並且可以利用Build Tool與Overlay Tool進行延伸與知識的拓展，以上各分析結果都是用來解釋實驗觀察到的現象的重要依據。

Regulator effect:將上下游之調控路徑整合

Analysis Match:比對外部實驗組資訊與實驗之調控相似相異性



Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Experiment Metadata

Analysis Settings

Top Canonical Pathways

Name

Superpathway of Cholesterol Biosynthesis

Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)

Mevalonate Pathway I

Cholesterol Biosynthesis I

IPA 分析結果

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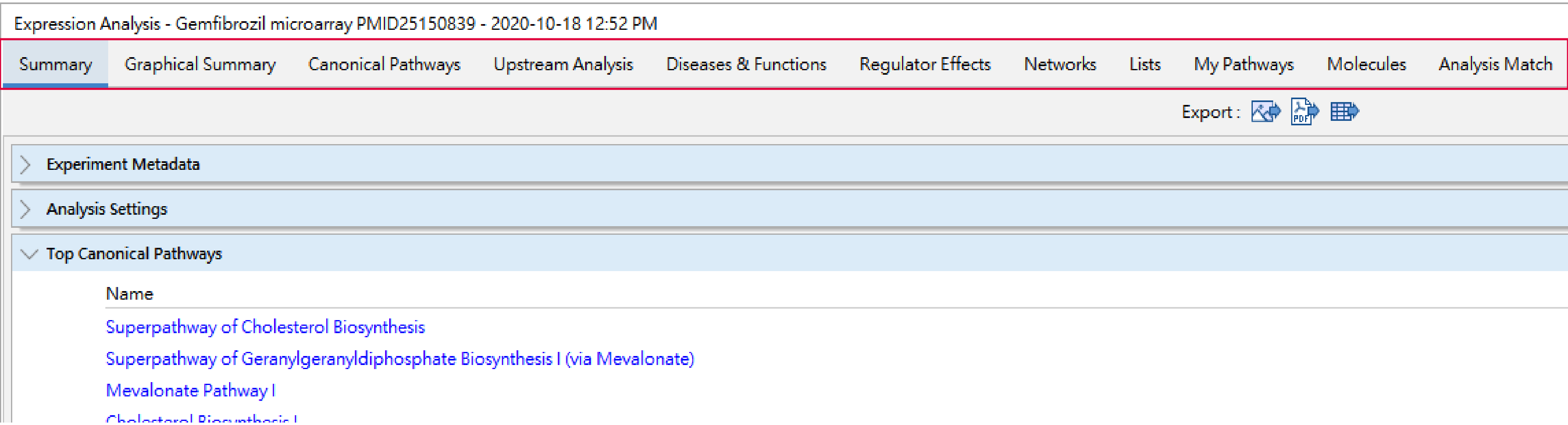
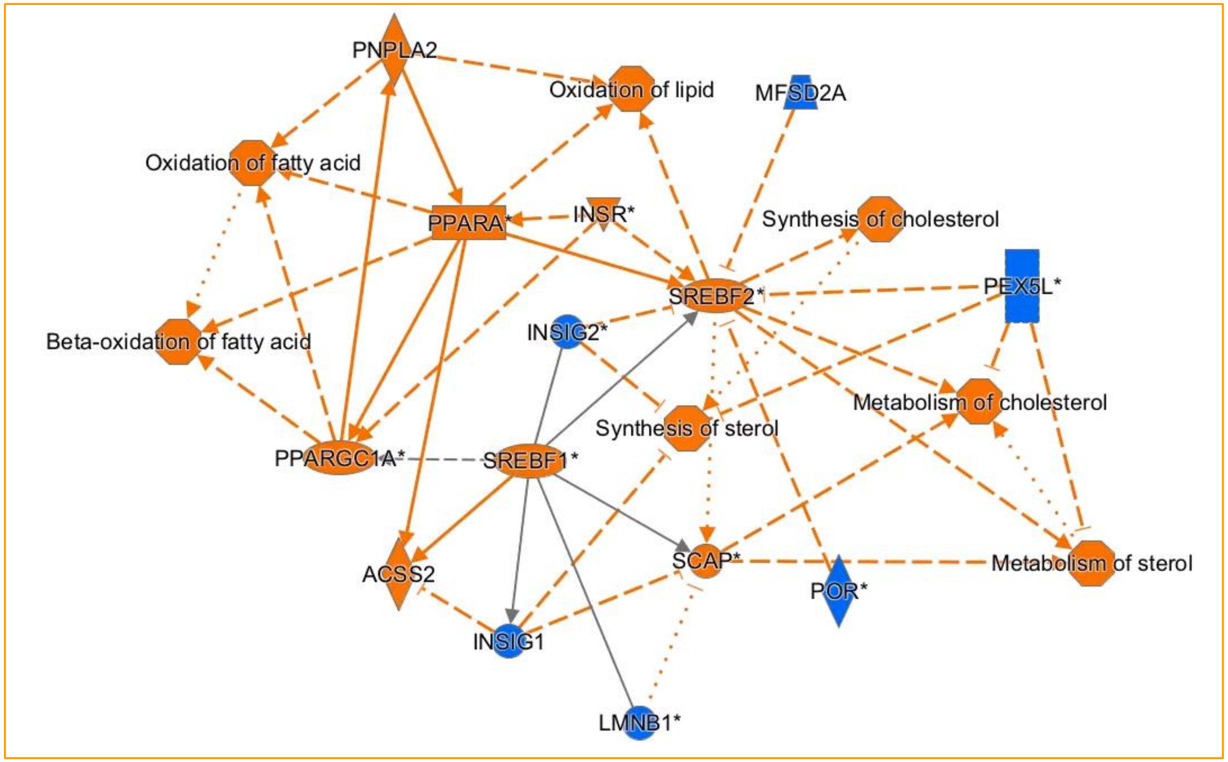

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Name
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Mevalonate Pathway I

Graphical Summary

Graphical Summary結果:
將資料集最相關的生物主題以網路圖像呈現
(canonical pathways, upstream regulators, causal network master regulators, diseases, and biological functions)



Criteria for selection

- □ All entities:
  p-value < 0.05
- □ Diseases、Functions、
  Upstream regulators:
  z-score≧2
- □ All molecules types
  (except chemicals)
- □ Activated nodes
  z-score≧2
- □ Inhibited nodes
  z-score≦-2

IPA 分析結果

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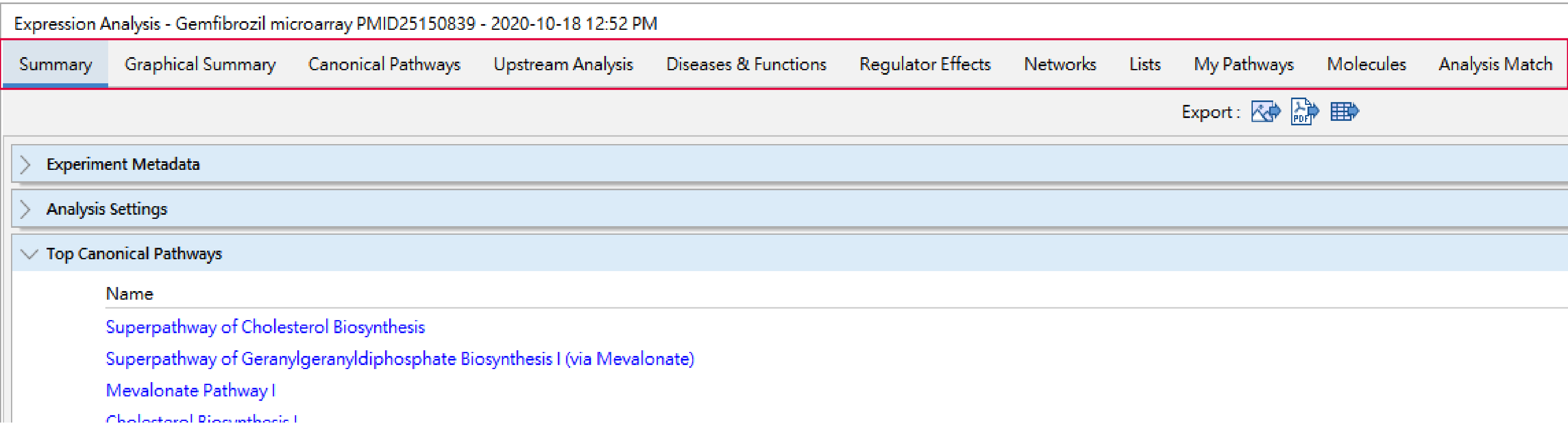

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Experiment Metadata

Analysis Settings

Top Canonical Pathways

Name
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Mevalonate Pathway I
Cholesterol Biosynthesis I

Canonical Pathway Analysis

Canonical Pathways結果標籤: 受影響的Signaling Pathway與Metabolic Pathway 依照顯著性用條狀圖**排列**

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

10 molecule(s) associated with **Cholesterol Biosynthesis III (via Desmosterol) at Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM** [Ratio: 10/13 (0.769)] [z-score: 3.16

點擊特定Canonical Pathway名稱上方的Bar條，下方視窗會出現dataset 中有參與組成該 pathway的分子 ID

IPA 分析結果

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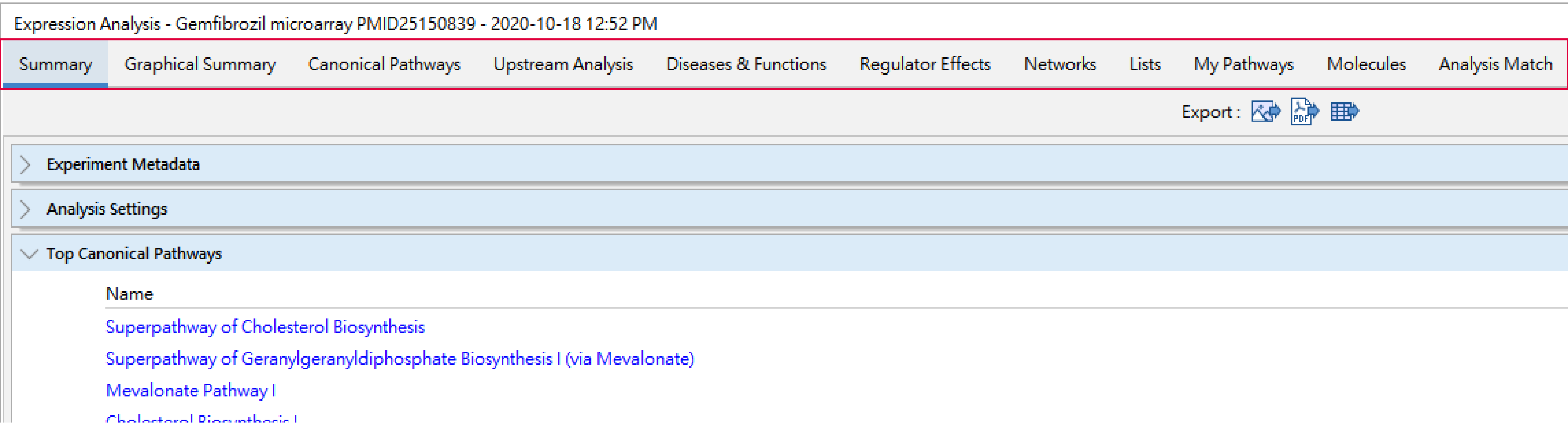

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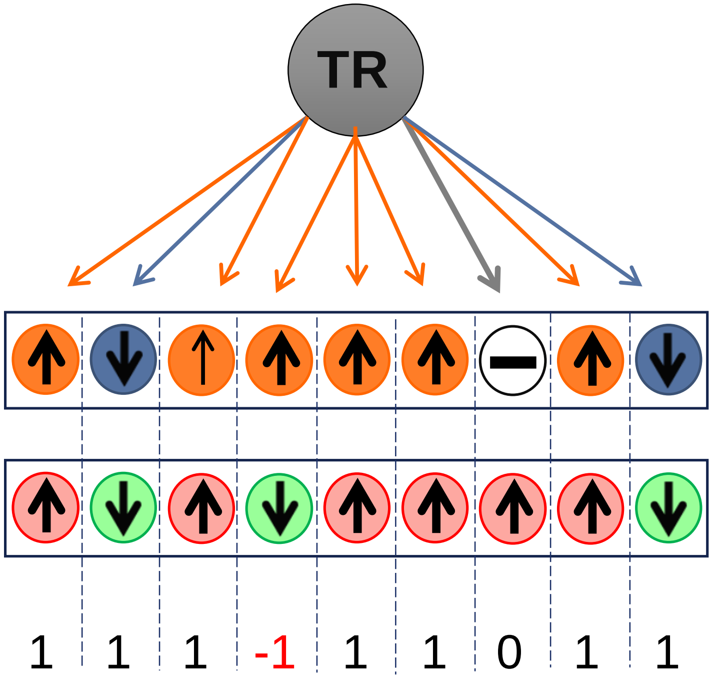
Upstream Analysis Activation z–score

Statistical measure of correlation between the transcription regulator (TR) and resulting gene expression



N = 8 genes

TR effect on downstream genes
(Literature)

Differential gene expression
(Uploaded Data)

z-score > 2 or < -2 is considered significant

Actual z-score *can* be weighted by relationship types, relationship bias, data bias

Upstream Analysis Activation z–score

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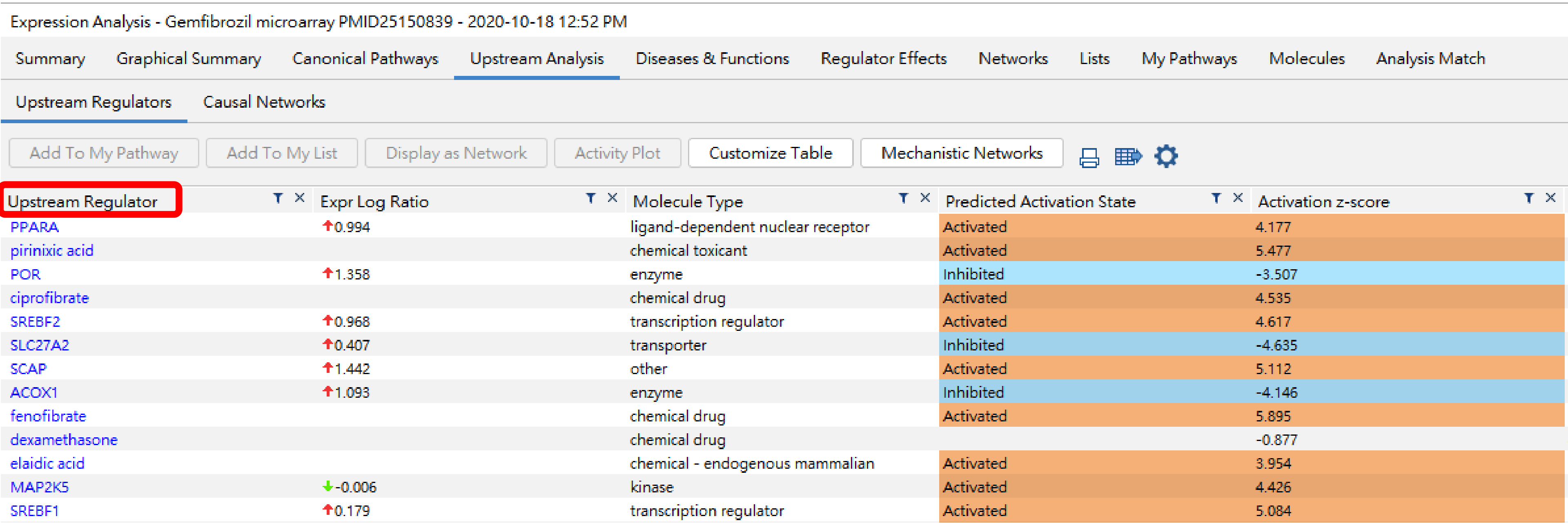

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score
PPARA	↑0.994	ligand-dependent nuclear receptor	Activated	4.177
pirinixic acid		chemical toxicant	Activated	5.477
POR	↑1.358	enzyme	Inhibited	-3.507
ciprofibrate		chemical drug	Activated	4.535
SREBF2	↑0.968	transcription regulator	Activated	4.617
SLC27A2	↑0.407	transporter	Inhibited	-4.635
SCAP	↑1.442	other	Activated	5.112
ACOX1	↑1.093	enzyme	Inhibited	-4.146
fenofibrate		chemical drug	Activated	5.895
dexamethasone		chemical drug		-0.877
elaidic acid		chemical - endogenous mammalian	Activated	3.954
MAP2K5	↓-0.006	kinase	Activated	4.426
SREBF1	↑0.179	transcription regulator	Activated	5.084

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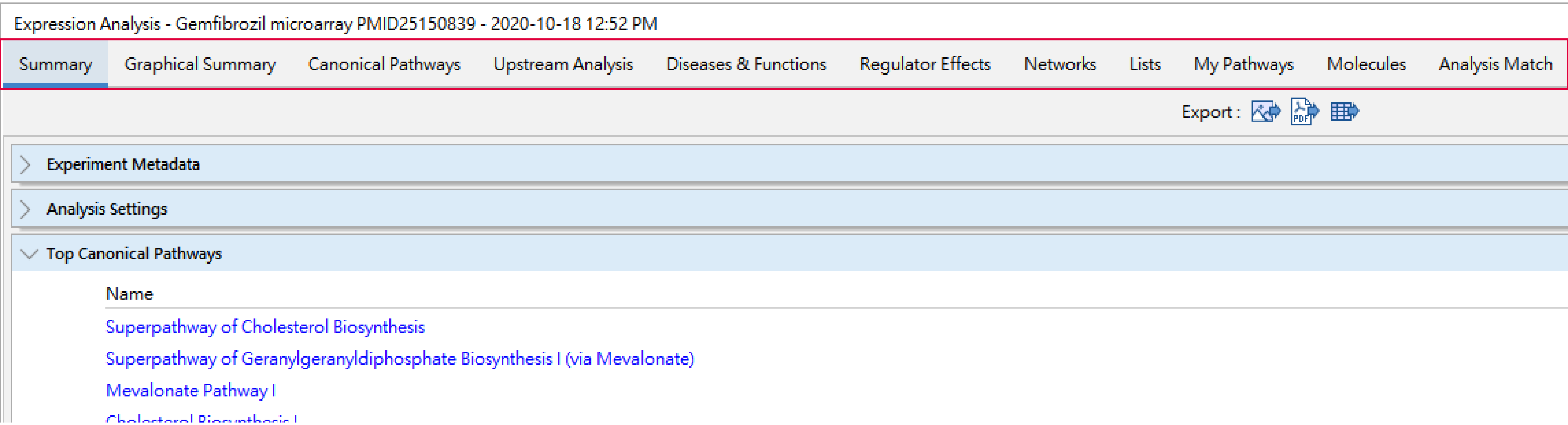

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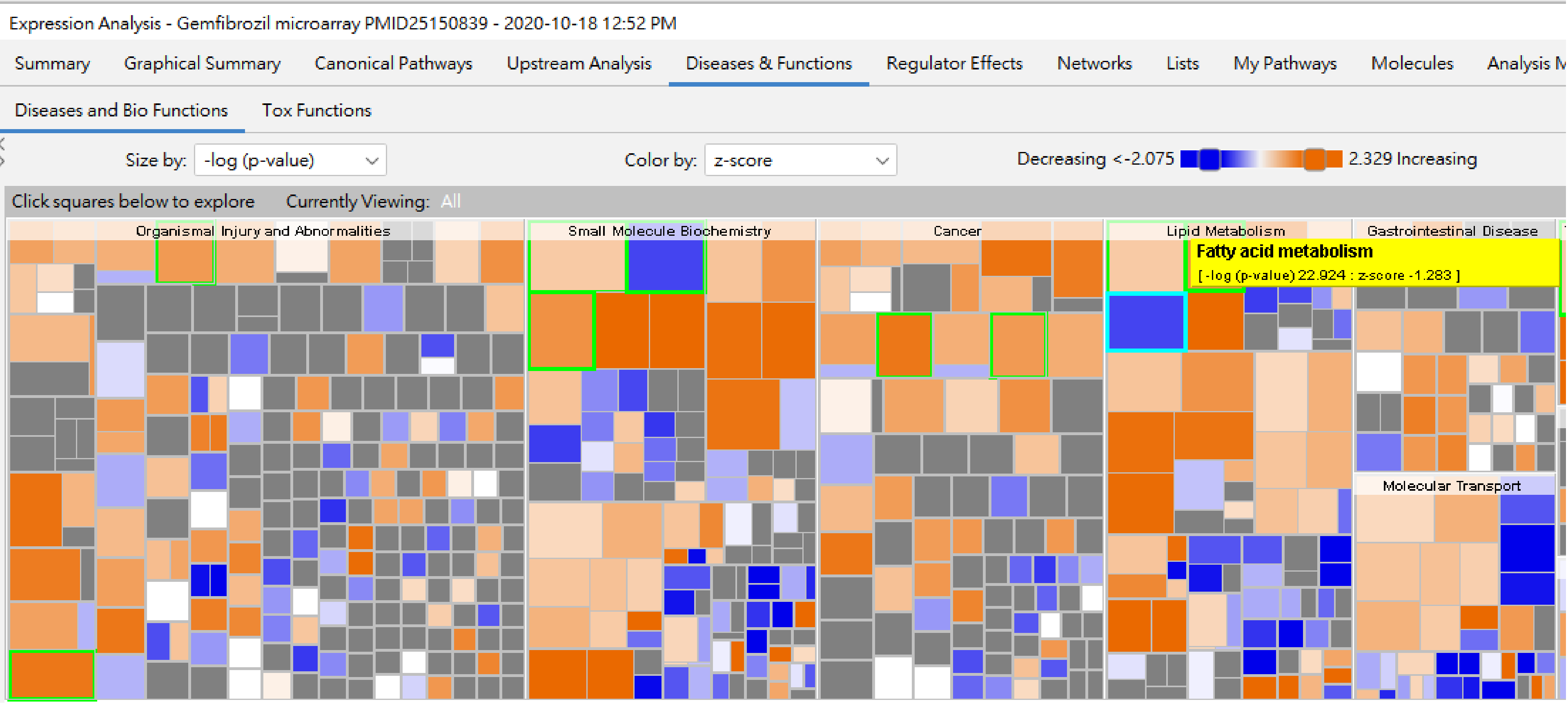
Diseases and functions

Diseases and functions結果標籤:
了解實驗結果在各分析疾病調控上之結果



Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Size by: -log (p-value)

Color by: z-score

Decreasing <-2.075 2.329 Increasing

Click squares below to explore Currently Viewing: All

Fatty acid metabolism
[-log (p-value) 22.924 : z-score -1.283]

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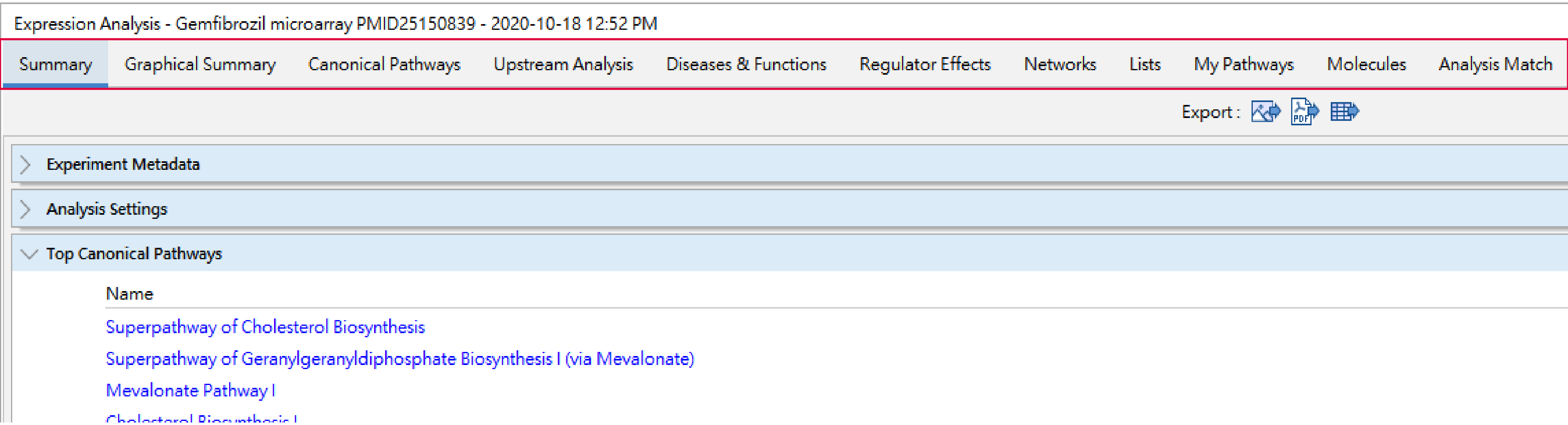

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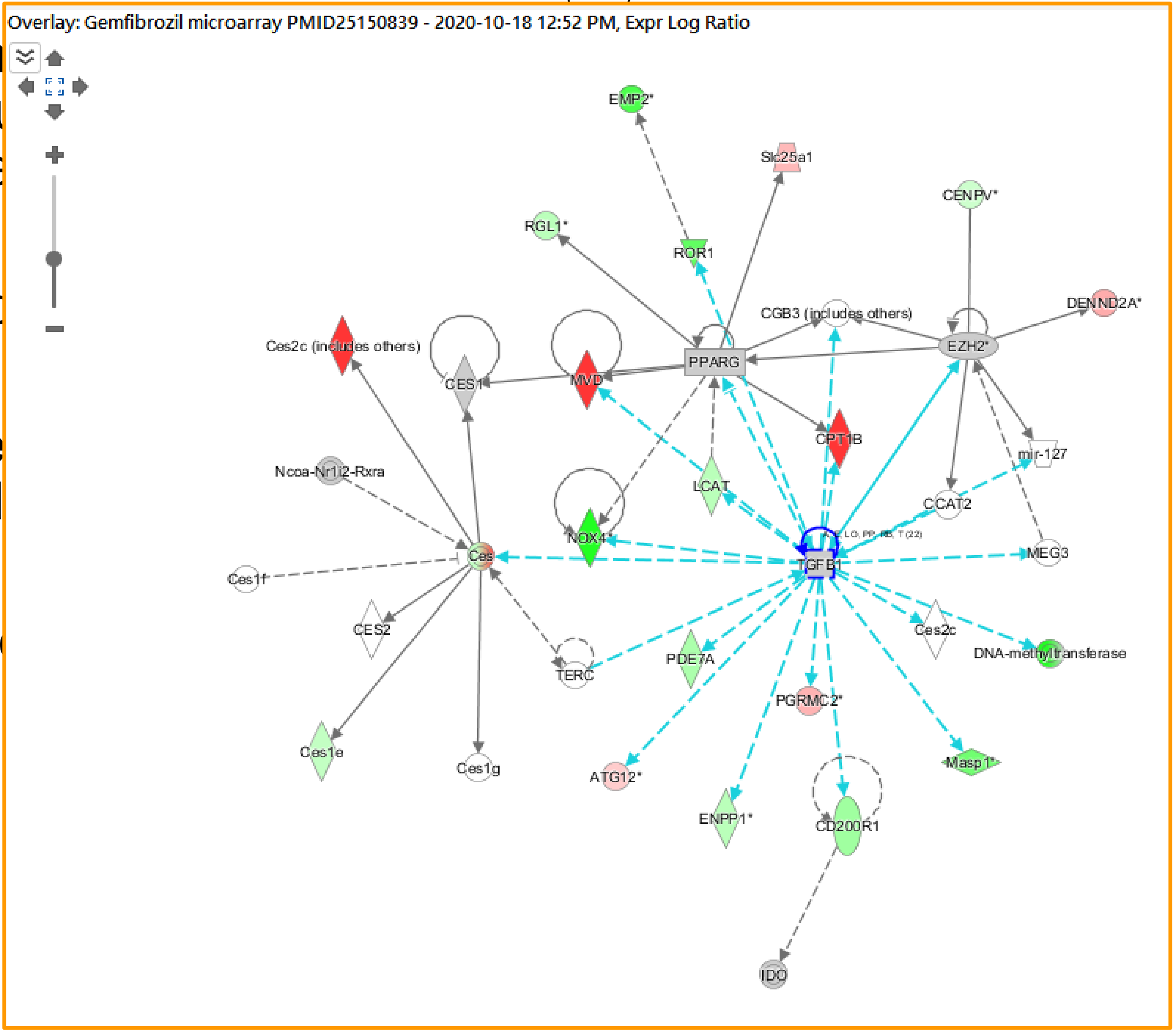
Mevalonate Pathway I

Cholesterol Biosynthesis I

How Networks Are Generated

1. Focus molecules are “seeds”
2. Focus molecules with th interactions to other focu are then connected toge network
3. Non-focus molecules fro dataset are then added
4. Molecules from the Inge Knowledge Base are ad
5. Resulting Networks are then sorted based on th



Overlay: Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM, Expr Log Ratio

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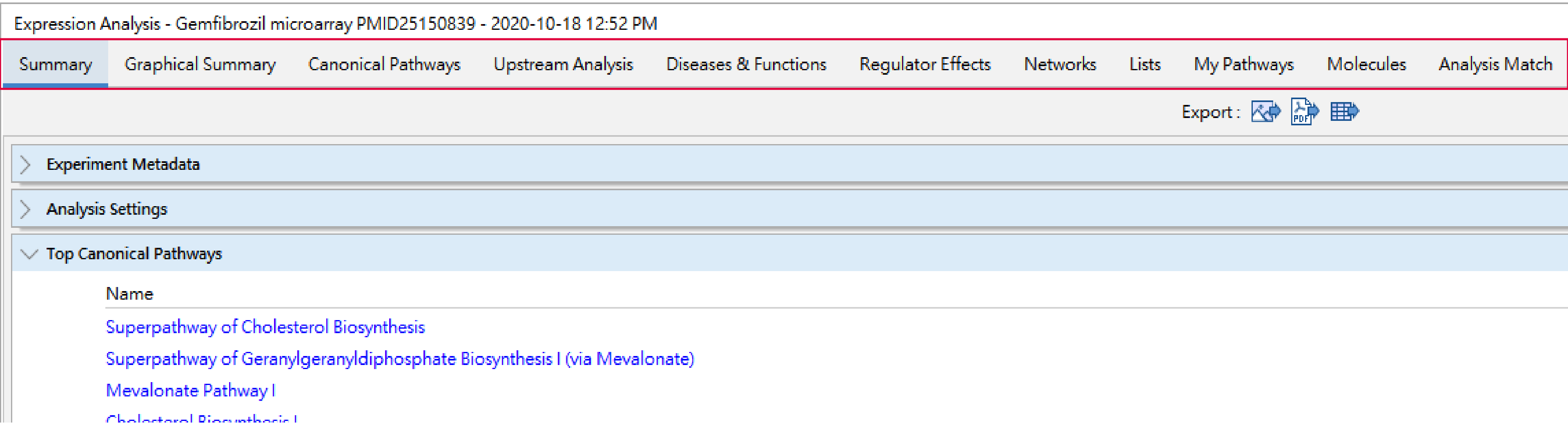

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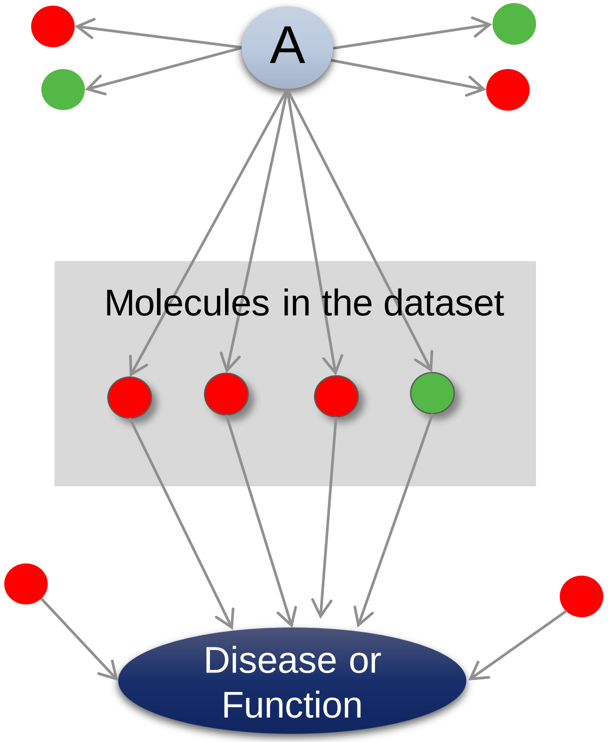
Concept of “Regulator Effects”

Hypotheses for how activated or inhibited upstream regulators cause downstream effects on biology

Upstream Regulators



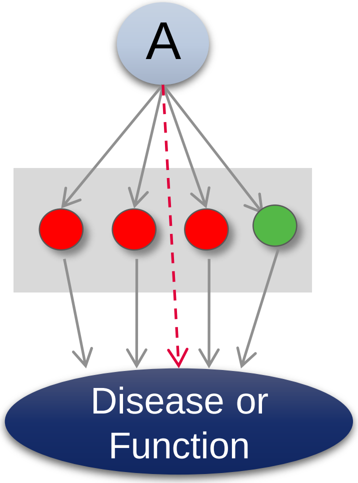
Downstream Effects Analysis

Algorithm

→

First iteration

Simplest Regulator Effects result



Displays a relationship between the regulator and disease/function if it exists

Causally consistent networks score higher

The algorithm runs iteratively to merge additional regulators with diseases and functions

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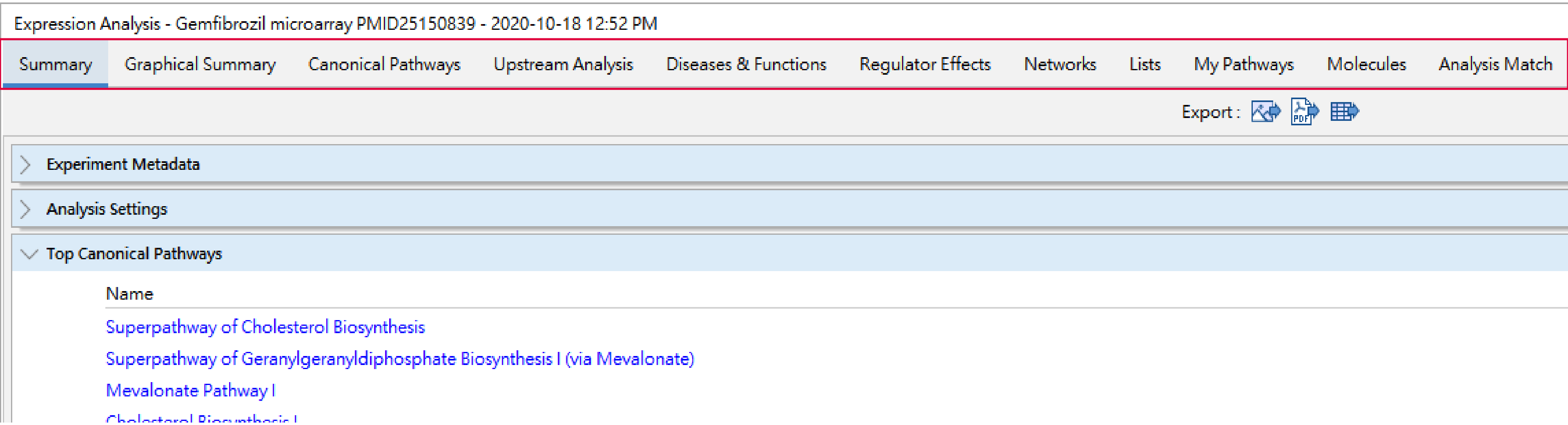
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Mevalonate Pathway I

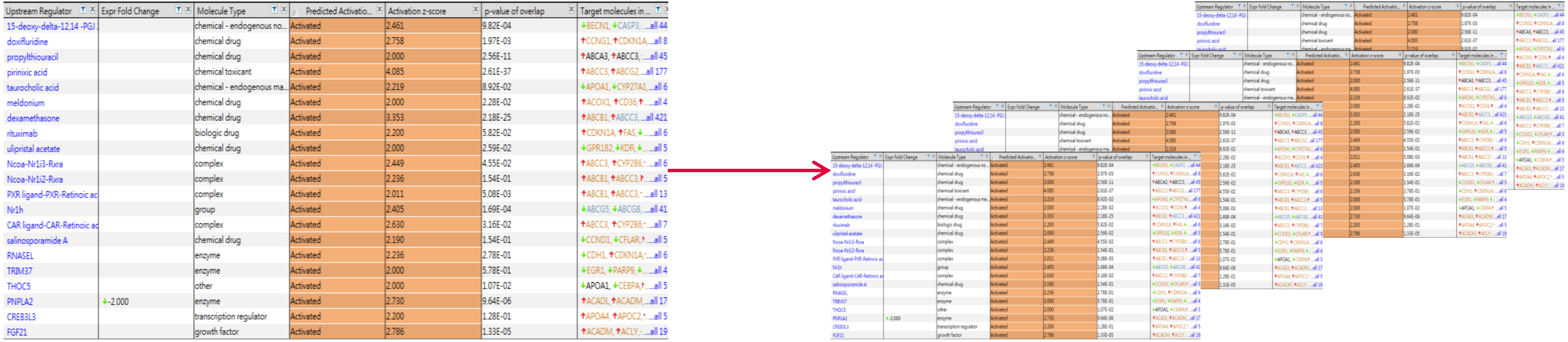
Sample to Insight

Analysis Match

Analysis Match enables you to automatically match your analysis against:

- All your own analysis
- Analyses of 8100+ expression datasets processed and curated from public sources by Omicsoft (QIAGEN)

- Build confidence in your analysis results
- Discover unexpected insights into mechanisms shared between studies
- Gain insight from ‘anti-matches’



Upstream Regulator	Expr Fold Change	Molecule Type	Predicted Activatio...	Activation z-score	p-value of overlap	Target molecules in ...
15-deoxy-delta-12,14 -PGJ		chemical - endogenous no...	Activated	2.461	9.82E-04	↓BECN1, ↓CASP3, ...all 44
doxifluridine		chemical drug	Activated	2.758	1.97E-03	↑CCNG1, ↑CDKN1A, ...all 8
propylthiouracil		chemical drug	Activated	2.000	2.56E-11	↑ABCA3, ↑ABCC3, ...all 45
pirinixic acid		chemical toxicant	Activated	4.085	2.61E-37	↑ABCC3, ↑ABCG2, ...all 177
taurocholic acid		chemical - endogenous ma...	Activated	2.219	8.92E-02	↓APOA1, ↓CYP27A1, ...all 6
meldonium		chemical drug	Activated	2.000	2.28E-02	↑ACOX1, ↑CD36, ↑...all 4
dexamethasone		chemical drug	Activated	3.353	2.18E-25	↑ABCB1, ↑ABCC3, ...all 421
rituximab		biologic drug	Activated	2.200	5.82E-02	↑CDKN1A, ↑FAS, ↓...all 6
ulipristal acetate		chemical drug	Activated	2.000	2.59E-02	↓GPR182, ↓KDR, ↓...all 5
Ncoa-Nr1i3-Rxra		complex	Activated	2.449	4.55E-02	↑ABCC3, ↑CYP2B6, ...all 6
Ncoa-Nr1i2-Rxra		complex	Activated	2.236	1.54E-01	↑ABCB1, ↑ABCC3, ↑...all 5
PXR ligand-PXR-Retinoic ac		complex	Activated	2.011	5.08E-03	↑ABCB1, ↑ABCC3, ...all 13
Nr1h		group	Activated	2.405	1.69E-04	↓ABCG5, ↓ABCG8, ...all 41
CAR ligand-CAR-Retinoic ac		complex	Activated	2.630	3.16E-02	↑ABCC3, ↑CYP2B6, ...all 7
salinosporamide A		chemical drug	Activated	2.190	1.54E-01	↓CCND1, ↓CFLAR, ↑...all 5
RNASEL		enzyme	Activated	2.236	2.78E-01	↓CDH1, ↑CDKN1A, ...all 6
TRIM37		enzyme	Activated	2.000	5.78E-01	↓EGR1, ↓PARP9, ↓...all 4
THOC5		other	Activated	2.000	1.07E-02	↓APOA1, ↓CEBPA, ↑...all 5
PNPLA2	↓-2.000	enzyme	Activated	2.730	9.64E-06	↑ACADL, ↑ACADM, ...all 17
CREB3L3		transcription regulator	Activated	2.200	1.28E-01	↑APOA4, ↑APOC2, ...all 5
FGF21		growth factor	Activated	2.786	1.33E-05	↑ACADM, ↑ACLY, ...all 19

Live Demo

Analysis Match

Unprecedented discovery, together

Array Express
GEO
SRA
TCGA
Etc.

Curation, Processing, & QA

Datasets integrated into OmicSoft Lands

OmicSoft
Array Suite

Journal articles

Clinical Trials
COSMIC
OMIM
MGD
Etc.

Curation & QA

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OncoLand
DiseaseLand

8100+ Expression comparison datasets

INGENUITY®
PATHWAY ANALYSIS

- Biological analyses of each dataset
- Compare your analysis to all OmicSoft analyses

Analysis Match

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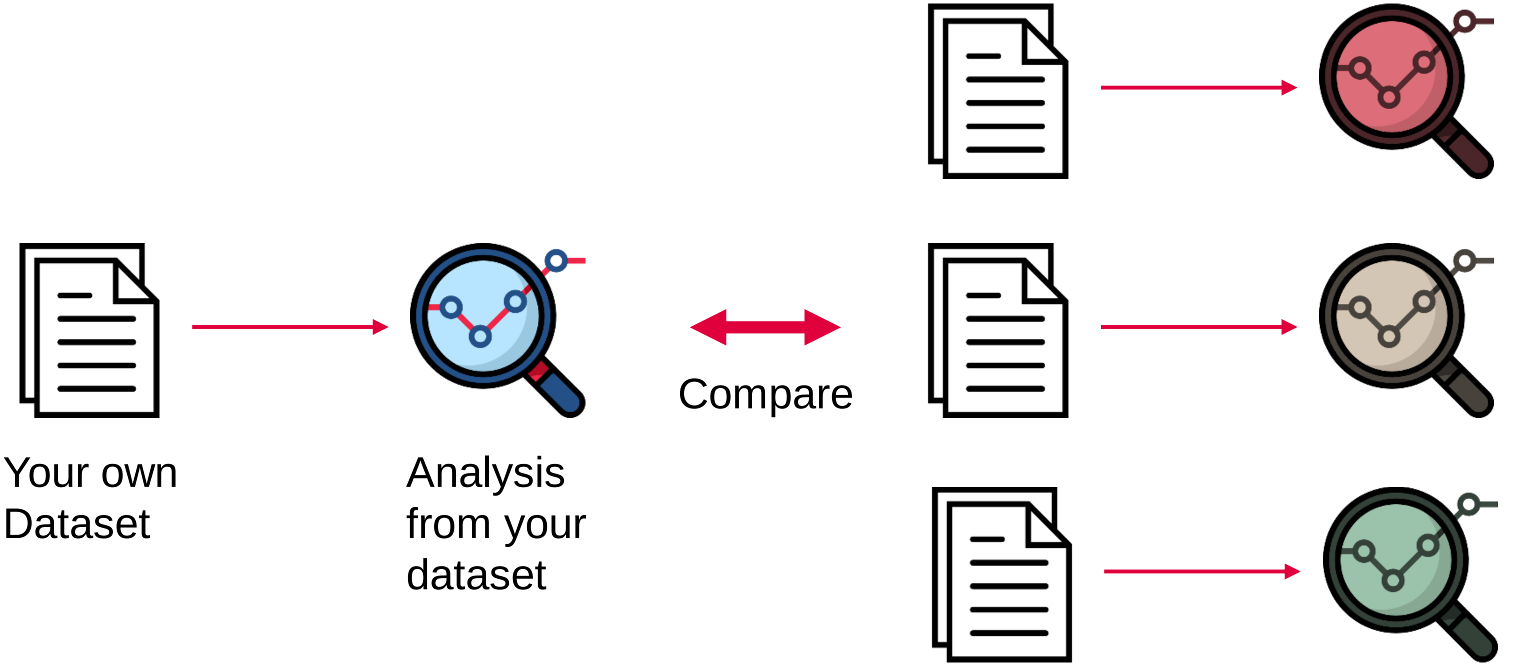
並自**LINCS（NIH Library of Integrated Network-Based Cellular Signatures）**再添加大約**28,000**個分析組，總數將超過**73,000**個



Your own Dataset

Analysis from your dataset

Compare

Donor Datasets

Analysis from donor datasets

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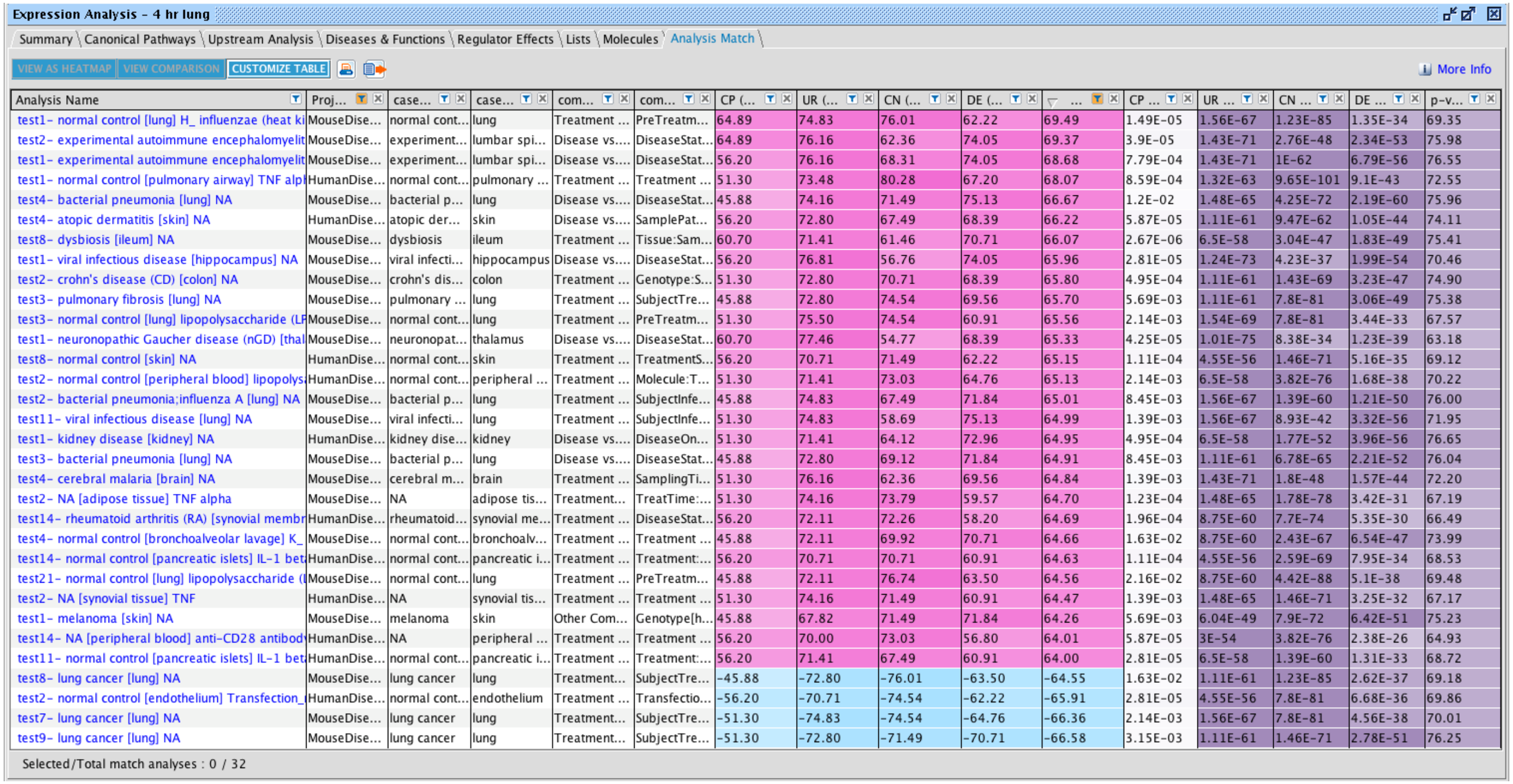
並自**DiseaseLand & OncoLand**再添加大約**6,900**個分析組，總數將超過**80,000**個!

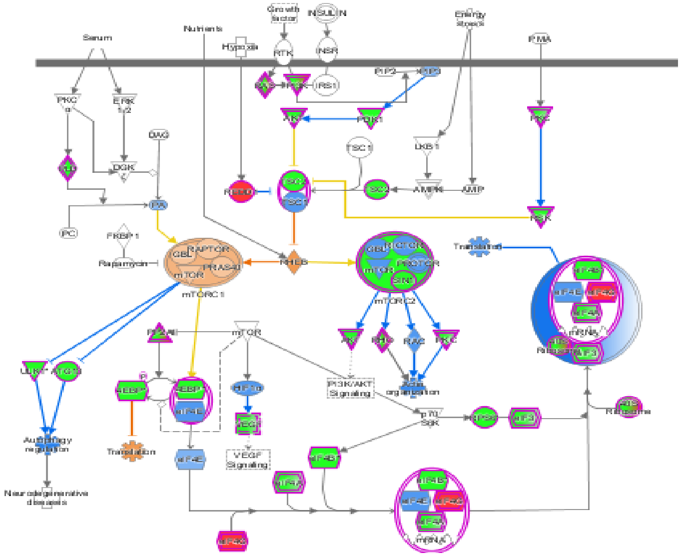


Analysis Name	Proj...	case...	case...	com...	com...	CP (...	UR (...	CN (...	DE (...	...	CP ...	UR ...	CN ...	DE ...	p-v...
test1- normal control [lung] H_ influenzae (heat ki	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	64.89	74.83	76.01	62.22	69.49	1.49E-05	1.56E-67	1.23E-85	1.35E-34	69.35
test2- experimental autoimmune encephalomyelit	MouseDise...	experiment...	lumbar spi...	Disease vs....	DiseaseStat...	64.89	76.16	62.36	74.05	69.37	3.9E-05	1.43E-71	2.76E-48	2.34E-53	75.98
test1- experimental autoimmune encephalomyelit	MouseDise...	experiment...	lumbar spi...	Disease vs....	DiseaseStat...	56.20	76.16	68.31	74.05	68.68	7.79E-04	1.43E-71	1E-62	6.79E-56	76.55
test1- normal control [pulmonary airway] TNF alpl	HumanDise...	normal cont...	pulmonary ...	Treatment ...	Treatment ...	51.30	73.48	80.28	67.20	68.07	8.59E-04	1.32E-63	9.65E-101	9.1E-43	72.55
test4- bacterial pneumonia [lung] NA	MouseDise...	bacterial p...	lung	Disease vs....	DiseaseStat...	45.88	74.16	71.49	75.13	66.67	1.2E-02	1.48E-65	4.25E-72	2.19E-60	75.96
test4- atopic dermatitis [skin] NA	HumanDise...	atopic der...	skin	Disease vs....	SamplePat...	56.20	72.80	67.49	68.39	66.22	5.87E-05	1.11E-61	9.47E-62	1.05E-44	74.11
test8- dysbiosis [ileum] NA	MouseDise...	dysbiosis	ileum	Treatment ...	Tissue:Sam...	60.70	71.41	61.46	70.71	66.07	2.67E-06	6.5E-58	3.04E-47	1.83E-49	75.41
test1- viral infectious disease [hippocampus] NA	MouseDise...	viral infecti...	hippocampus	Disease vs....	DiseaseStat...	56.20	76.81	56.76	74.05	65.96	2.81E-05	1.24E-73	4.23E-37	1.99E-54	70.46
test2- crohn's disease (CD) [colon] NA	MouseDise...	crohn's dis...	colon	Treatment ...	Genotype:S...	51.30	72.80	70.71	68.39	65.80	4.95E-04	1.11E-61	1.43E-69	3.23E-47	74.90
test3- pulmonary fibrosis [lung] NA	MouseDise...	pulmonary ...	lung	Treatment ...	SubjectTre...	45.88	72.80	74.54	69.56	65.70	5.69E-03	1.11E-61	7.8E-81	3.06E-49	75.38
test3- normal control [lung] lipopolysaccharide (LF	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	51.30	75.50	74.54	60.91	65.56	2.14E-03	1.54E-69	7.8E-81	3.44E-33	67.57
test1- neuronopathic Gaucher disease (nGD) [thal	MouseDise...	neuronopat...	thalamus	Disease vs....	DiseaseStat...	60.70	77.46	54.77	68.39	65.33	4.25E-05	1.01E-75	8.38E-34	1.23E-39	63.18
test8- normal control [skin] NA	HumanDise...	normal cont...	skin	Treatment ...	TreatmentS...	56.20	70.71	71.49	62.22	65.15	1.11E-04	4.55E-56	1.46E-71	5.16E-35	69.12
test2- normal control [peripheral blood] lipopolys	HumanDise...	normal cont...	peripheral ...	Treatment ...	Molecule:T...	51.30	71.41	73.03	64.76	65.13	2.14E-03	6.5E-58	3.82E-76	1.68E-38	70.22
test2- bacterial pneumonia;influenza A [lung] NA	MouseDise...	bacterial p...	lung	Treatment ...	SubjectInfe...	45.88	74.83	67.49	71.84	65.01	8.45E-03	1.56E-67	1.39E-60	1.21E-50	76.00
test11- viral infectious disease [lung] NA	MouseDise...	viral infecti...	lung	Treatment ...	SubjectInfe...	51.30	74.83	58.69	75.13	64.99	1.39E-03	1.56E-67	8.93E-42	3.32E-56	71.95
test1- kidney disease [kidney] NA	HumanDise...	kidney dise...	kidney	Disease vs....	DiseaseOn...	51.30	71.41	64.12	72.96	64.95	4.95E-04	6.5E-58	1.77E-52	3.96E-56	76.65
test3- bacterial pneumonia [lung] NA	MouseDise...	bacterial p...	lung	Disease vs....	DiseaseStat...	45.88	72.80	69.12	71.84	64.91	8.45E-03	1.11E-61	6.78E-65	2.21E-52	76.04
test4- cerebral malaria [brain] NA	MouseDise...	cerebral m...	brain	Treatment ...	SamplingTi...	51.30	76.16	62.36	69.56	64.84	1.39E-03	1.43E-71	1.8E-48	1.57E-44	72.20
test2- NA [adipose tissue] TNF alpha	MouseDise...	NA	adipose tis...	Treatment...	TreatTime:...	51.30	74.16	73.79	59.57	64.70	1.23E-04	1.48E-65	1.78E-78	3.42E-31	67.19
test14- rheumatoid arthritis (RA) [synovial membr	HumanDise...	rheumatoid...	synovial me...	Treatment ...	DiseaseStat...	56.20	72.11	72.26	58.20	64.69	1.96E-04	8.75E-60	7.7E-74	5.35E-30	66.49
test4- normal control [bronchoalveolar lavage] K_	MouseDise...	normal cont...	bronchoalv...	Treatment ...	Treatment ...	45.88	72.11	69.92	70.71	64.66	1.63E-02	8.75E-60	2.43E-67	6.54E-47	73.99
test14- normal control [pancreatic islets] IL-1 bet	HumanDise...	normal cont...	pancreatic i...	Treatment ...	Treatment:...	56.20	70.71	70.71	60.91	64.63	1.11E-04	4.55E-56	2.59E-69	7.95E-34	68.53
test21- normal control [lung] lipopolysaccharide (l	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	45.88	72.11	76.74	63.50	64.56	2.16E-02	8.75E-60	4.42E-88	5.1E-38	69.48
test2- NA [synovial tissue] TNF	HumanDise...	NA	synovial tis...	Treatment ...	Treatment ...	51.30	74.16	71.49	60.91	64.47	1.39E-03	1.48E-65	1.46E-71	3.25E-32	67.17
test1- melanoma [skin] NA	MouseDise...	melanoma	skin	Other Com...	Genotype[h...	45.88	67.82	71.49	71.84	64.26	5.69E-03	6.04E-49	7.9E-72	6.42E-51	75.23
test14- NA [peripheral blood] anti-CD28 antibod	HumanDise...	NA	peripheral ...	Treatment ...	Treatment ...	56.20	70.00	73.03	56.80	64.01	5.87E-05	3E-54	3.82E-76	2.38E-26	64.93
test11- normal control [pancreatic islets] IL-1 bet	HumanDise...	normal cont...	pancreatic i...	Treatment ...	Treatment:...	56.20	71.41	67.49	60.91	64.00	2.81E-05	6.5E-58	1.39E-60	1.31E-33	68.72
test8- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-45.88	-72.80	-76.01	-63.50	-64.55	1.63E-02	1.11E-61	1.23E-85	2.62E-37	69.18
test2- normal control [endothelium] Transfection_	HumanDise...	normal cont...	endothelium	Treatment ...	Transfectio...	-56.20	-70.71	-74.54	-62.22	-65.91	2.81E-05	4.55E-56	7.8E-81	6.68E-36	69.86
test7- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-51.30	-74.83	-74.54	-64.76	-66.36	2.14E-03	1.56E-67	7.8E-81	4.56E-38	70.01
test9- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-51.30	-72.80	-71.49	-70.71	-66.58	3.15E-03	1.11E-61	1.46E-71	2.78E-51	76.25

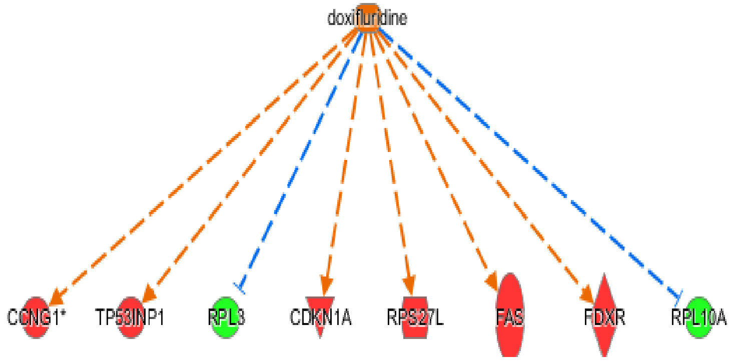
Selected/Total match analyses : 0 / 32

Analysis Match ‘Entities’

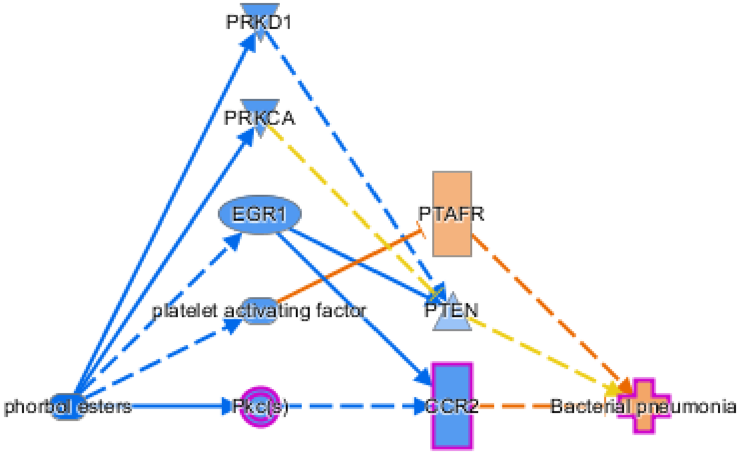
Canonical pathways (CP)



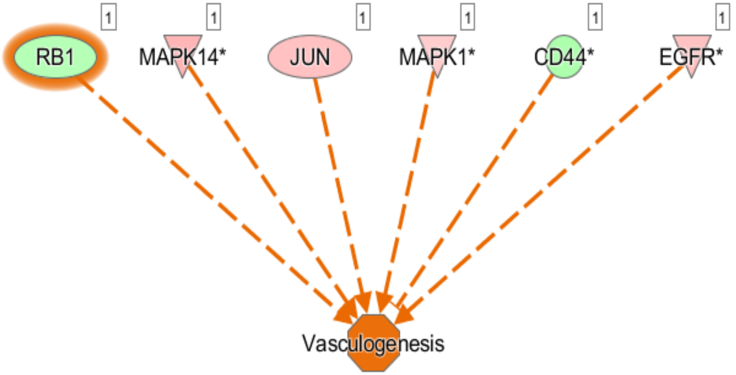
Upstream regulators (UR)



Causal networks (CN ‘master’ regulator)



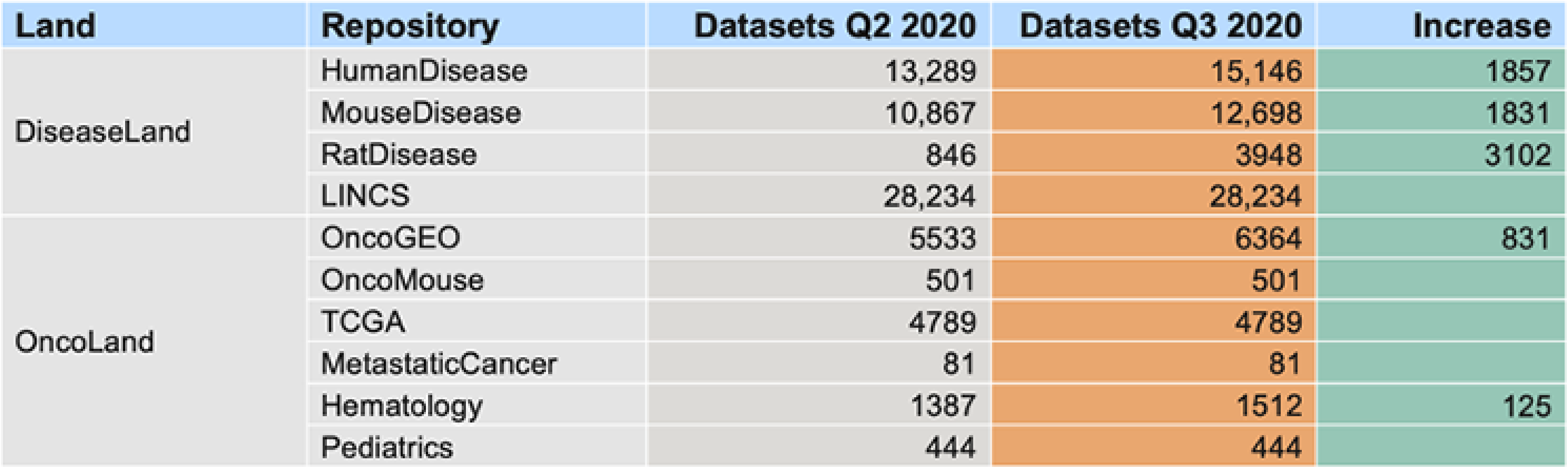
Disease and functions (DE)



Sample to Insight

Analysis Match Database

>73,000 OmicSoft Analyses available in Analysis Match and Activity Plot



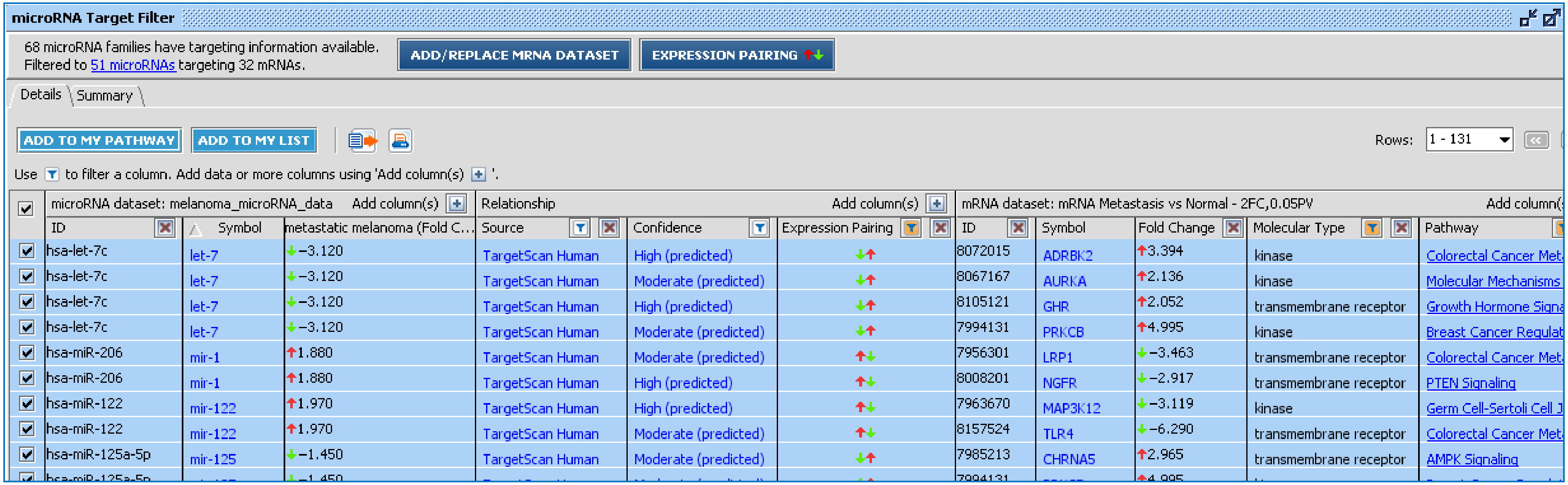
Land	Repository	Datasets Q2 2020	Datasets Q3 2020	Increase
DiseaseLand	HumanDisease	13,289	15,146	1857
	MouseDisease	10,867	12,698	1831
	RatDisease	846	3948	3102
	LINCS	28,234	28,234	
OncoLand	OncoGEO	5533	6364	831
	OncoMouse	501	501	
	TCGA	4789	4789	
	MetastaticCancer	81	81	
	Hematology	1387	1512	125
	Pediatrics	444	444	

OmicSoft analysis content in Analysis Match and Activity Plot. More than 7,700 new analyses have been added in this release.

Live Demo

microRNA target filter

Filter Datasets for Biomarkers or miRNA Targets



68 microRNA families have targeting information available.
Filtered to 51 microRNAs targeting 32 mRNAs.

Use to filter a column. Add data or more columns using 'Add column(s) '.

☑	microRNA dataset: melanoma_microRNA_data			Relationship			mRNA dataset: mRNA Metastasis vs Normal - 2FC,0.05PV				
	ID	Symbol	metastatic melanoma (Fold C...	Source	Confidence	Expression Pairing	ID	Symbol	Fold Change	Molecular Type	Pathway
☑	hsa-let-7c	let-7	↓−3.120	TargetScan Human	High (predicted)	↓↑	8072015	ADRBK2	↑3.394	kinase	Colorectal Cancer Met
☑	hsa-let-7c	let-7	↓−3.120	TargetScan Human	Moderate (predicted)	↓↑	8067167	AURKA	↑2.136	kinase	Molecular Mechanisms
☑	hsa-let-7c	let-7	↓−3.120	TargetScan Human	High (predicted)	↓↑	8105121	GHR	↑2.052	transmembrane receptor	Growth Hormone Signa
☑	hsa-let-7c	let-7	↓−3.120	TargetScan Human	Moderate (predicted)	↓↑	7994131	PRKCB	↑4.995	kinase	Breast Cancer Regulat
☑	hsa-miR-206	mir-1	↑1.880	TargetScan Human	Moderate (predicted)	↑↓	7956301	LRP1	↓−3.463	transmembrane receptor	Colorectal Cancer Met
☑	hsa-miR-206	mir-1	↑1.880	TargetScan Human	High (predicted)	↑↓	8008201	NGFR	↓−2.917	transmembrane receptor	PTEN Signaling
☑	hsa-miR-122	mir-122	↑1.970	TargetScan Human	High (predicted)	↑↓	7963670	MAP3K12	↓−3.119	kinase	Germ Cell-Sertoli Cell J
☑	hsa-miR-122	mir-122	↑1.970	TargetScan Human	Moderate (predicted)	↑↓	8157524	TLR4	↓−6.290	transmembrane receptor	Colorectal Cancer Met
☑	hsa-miR-125a-5p	mir-125	↓−1.450	TargetScan Human	Moderate (predicted)	↓↑	7985213	CHRNA5	↑2.965	transmembrane receptor	AMPK Signaling
☑	hsa-miR-125a-5p		↓−1.450				7994131		↑4.995		

88 data points

13,690 targets

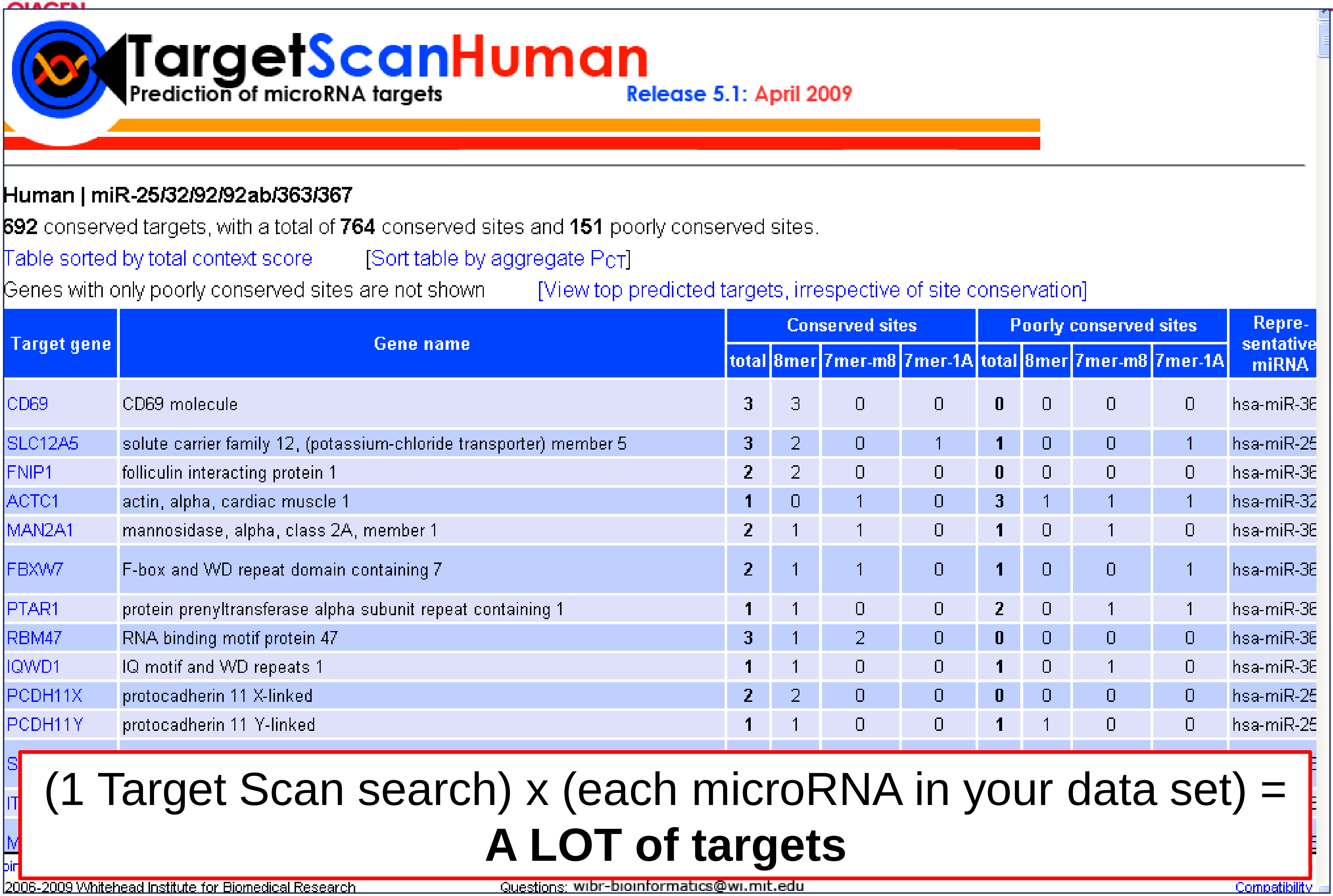
1,090 targets

333 targets

39 targets

32 targets

Use Pathway tools to build hypothesis for microRNA to mRNA target association



TargetScanHuman

Prediction of microRNA targets

Release 5.1: April 2009

Human | miR-25/32/92/92ab/363/367

692 conserved targets, with a total of **764** conserved sites and **151** poorly conserved sites.

Table sorted by total context score [Sort table by aggregate P_{CT}]

Genes with only poorly conserved sites are not shown [View top predicted targets, irrespective of site conservation]

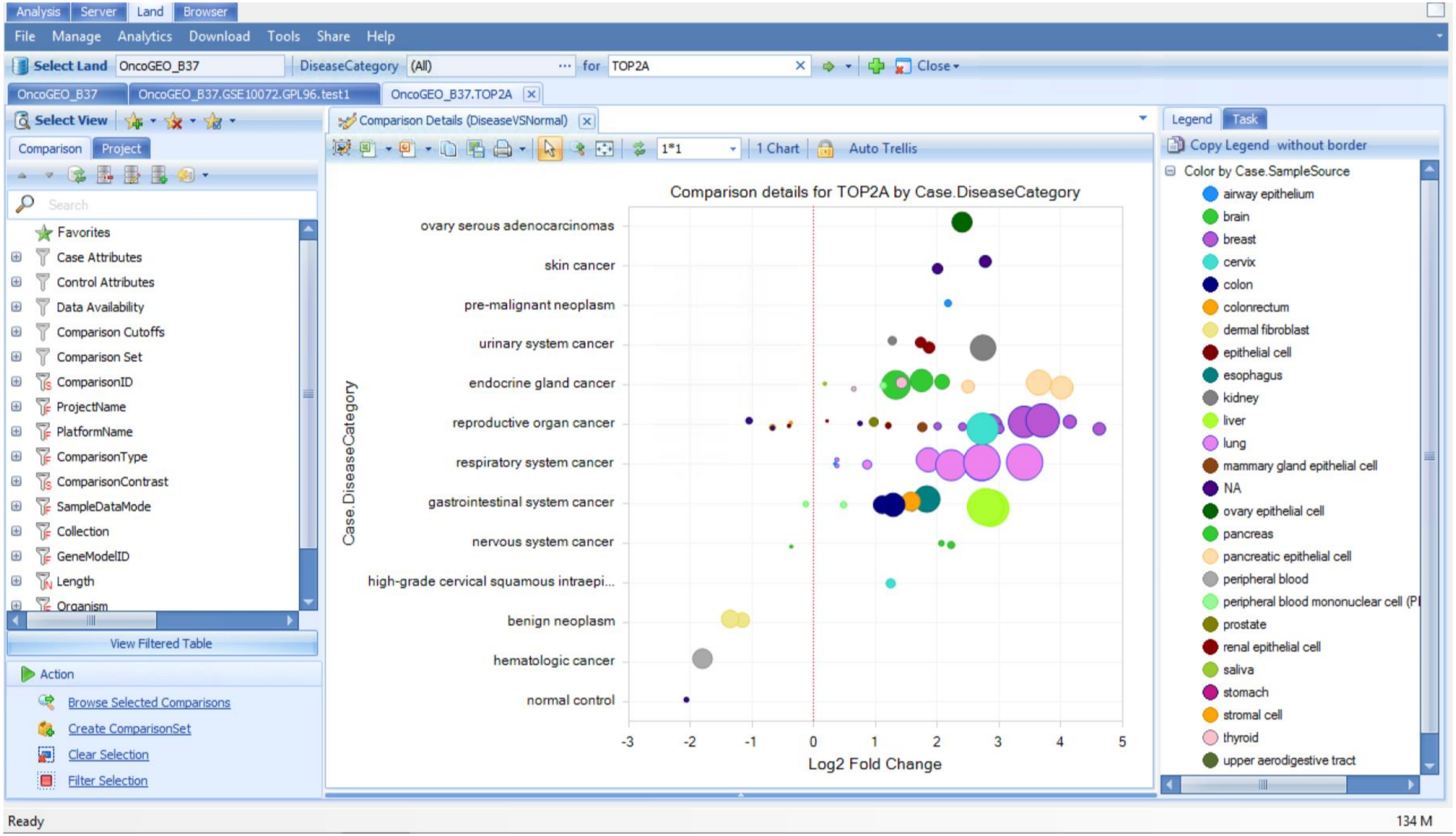
Target gene	Gene name	Conserved sites				Poorly conserved sites				Repre-sentative miRNA
		total	8mer	7mer-m8	7mer-1A	total	8mer	7mer-m8	7mer-1A	
CD69	CD69 molecule	**3**	3	0	0	**0**	0	0	0	hsa-miR-36
SLC12A5	solute carrier family 12, (potassium-chloride transporter) member 5	**3**	2	0	1	**1**	0	0	1	hsa-miR-25
FNIP1	folliculin interacting protein 1	**2**	2	0	0	**0**	0	0	0	hsa-miR-36
ACTC1	actin, alpha, cardiac muscle 1	**1**	0	1	0	**3**	1	1	1	hsa-miR-32
MAN2A1	mannosidase, alpha, class 2A, member 1	**2**	1	1	0	**1**	0	1	0	hsa-miR-36
FBXW7	F-box and WD repeat domain containing 7	**2**	1	1	0	**1**	0	0	1	hsa-miR-36
PTAR1	protein prenyltransferase alpha subunit repeat containing 1	**1**	1	0	0	**2**	0	1	1	hsa-miR-36
RBM47	RNA binding motif protein 47	**3**	1	2	0	**0**	0	0	0	hsa-miR-36
IQWD1	IQ motif and WD repeats 1	**1**	1	0	0	**1**	0	1	0	hsa-miR-36
PCDH11X	protocadherin 11 X-linked	**2**	2	0	0	**0**	0	0	0	hsa-miR-25
PCDH11Y	protocadherin 11 Y-linked	**1**	1	0	0	**1**	1	0	0	hsa-miR-25

2006-2009 Whitehead Institute for Biomedical Research Questions: wibr-bioinformatics@wi.mit.edu Compatibility

(1 Target Scan search) x (each microRNA in your data set) =
A LOT of targets

OmicSoft Array Suite provides detailed view of underlying data

Visualizing an individual gene across comparisons



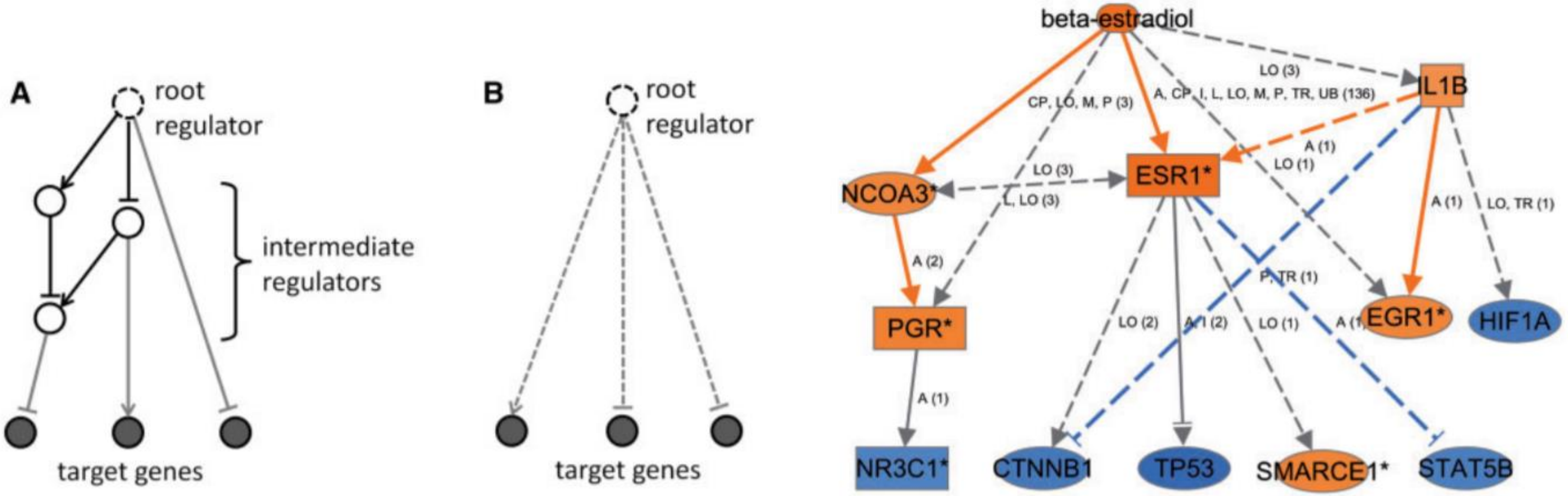
Select Land: OncoGEO_B37
DiseaseCategory: (All)
for: TOP2A

Live Demo

Causal Network

Causal Network

The enhanced Causal Network Analysis (CNA) provides a comprehensive approach to identifying upstream molecules that control the expression of the genes in your datasets. You can now, in a single click, visualize the diseases and functions you are scoring against, understand the effect of the master regulator on that disease or function, and drill-down to the evidence supporting those relationships. In addition, increase the predictive power by allowing intervening molecules or functions, up to three steps or 'hops', to connect a hypothesis to the scoring criteria.

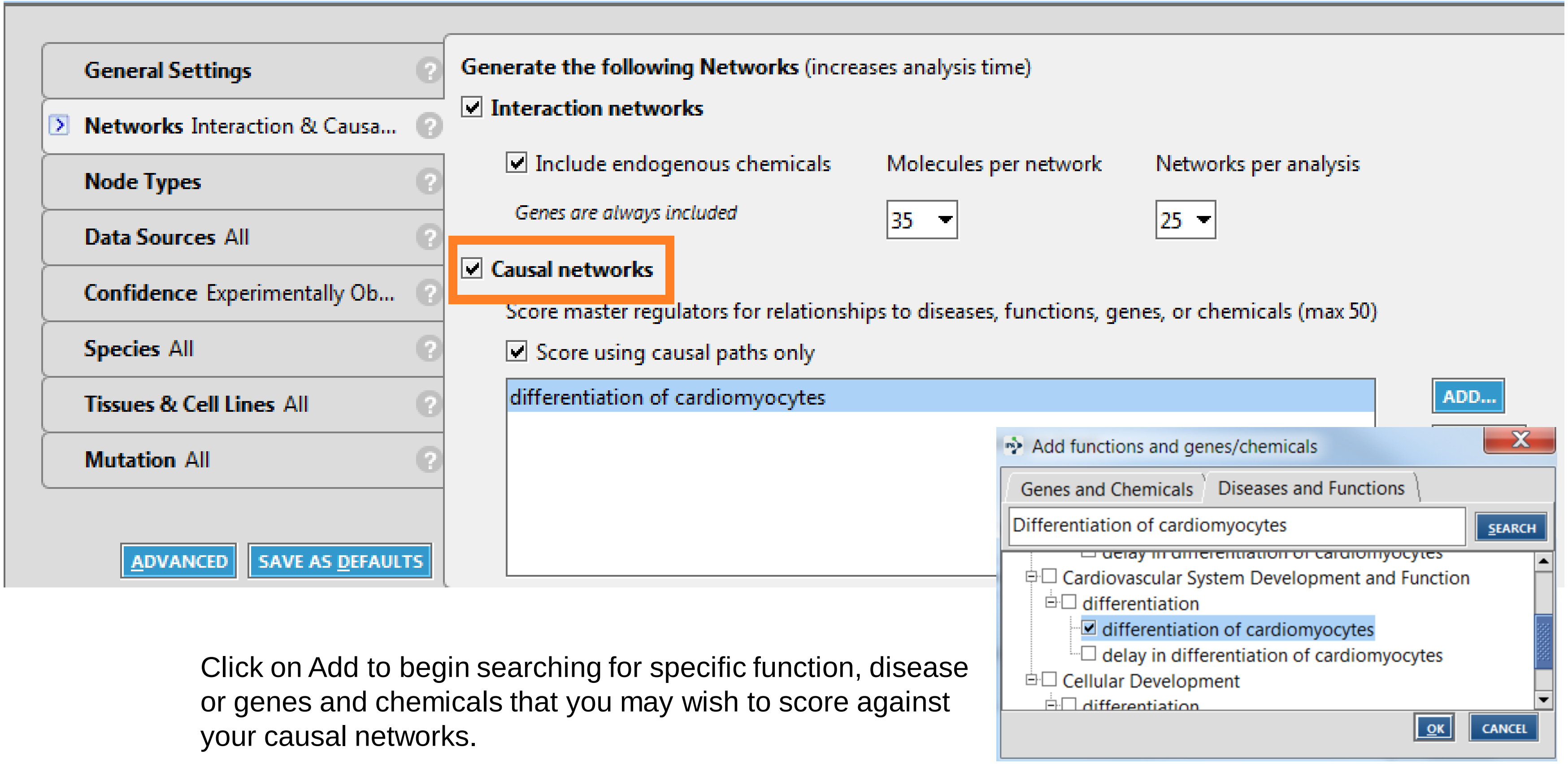


Causal analysis approaches in Ingenuity Pathway Analysis. 2014 *Bioinformatics*

Causal Network

How to Create Causal networks?

The option to build causal networks is available in IPA on the Create Analysis page. Select the check box for Causal network under General Settings > Networks to include Casual Analysis in your analysis results.



General Settings

Networks Interaction & Causa...

Node Types

Data Sources All

Confidence Experimentally Ob...

Species All

Tissues & Cell Lines All

Mutation All

Generate the following Networks (increases analysis time)

☑ **Interaction networks**

☑ Include endogenous chemicals

Genes are always included

Molecules per network: 35

Networks per analysis: 25

☑ **Causal networks**

Score master regulators for relationships to diseases, functions, genes, or chemicals (max 50)

☑ Score using causal paths only

differentiation of cardiomyocytes

Add functions and genes/chemicals

Differentiation of cardiomyocytes

☐ delay in differentiation of cardiomyocytes
☐ Cardiovascular System Development and Function
  ☐ differentiation
    ☑ differentiation of cardiomyocytes
    ☐ delay in differentiation of cardiomyocytes
☐ Cellular Development
  ☐ differentiation

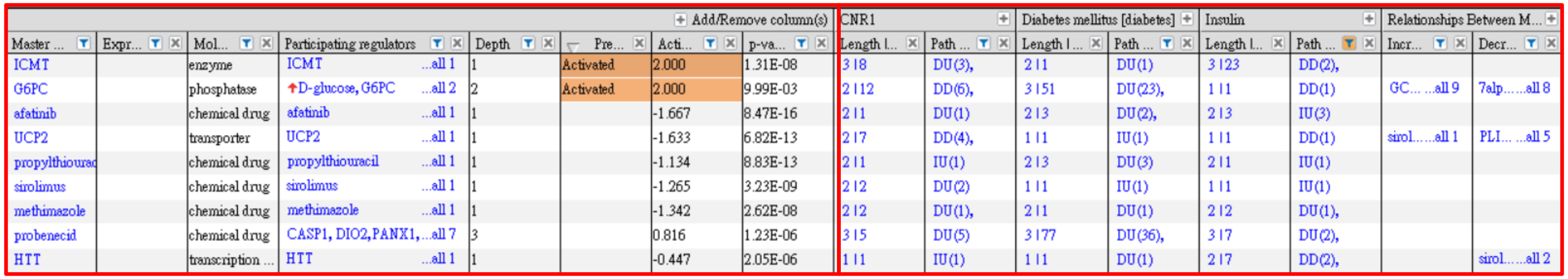
Click on Add to begin searching for specific function, disease or genes and chemicals that you may wish to score against your causal networks.

Causal Network

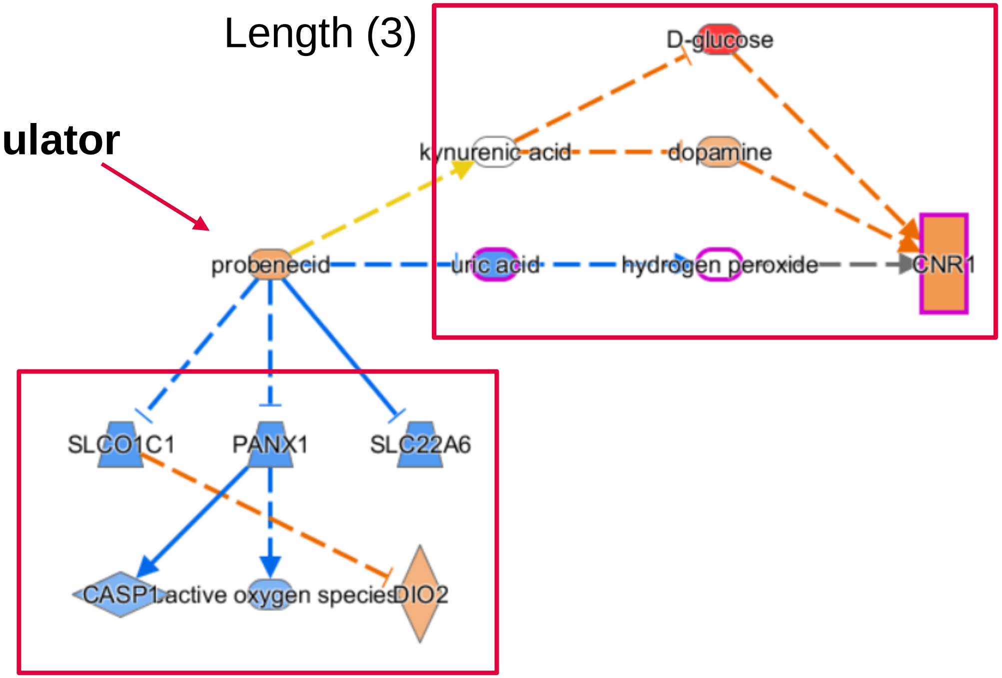
Result

Specific function, disease or genes and chemicals that you wish to score against your causal networks.

Master Regulator and Networks



Add/Remove column(s)								CNR1		Diabetes mellitus [diabetes]		Insulin		Relationships Between M...	
Master ...	Expr...	Mol...	Participating regulators	Depth	Pre...	Acti...	p-va...	Length l...	Path ...	Length l...	Path ...	Length l...	Path ...	Incr...	Decr...
ICMT		enzyme	ICMT ...all 1	1	Activated	2.000	1.31E-08	3 | 8	DU(3),	2 | 1	DU(1)	3 | 23	DD(2),		
G6PC		phosphatase	↑D-glucose, G6PC ...all 2	2	Activated	2.000	9.99E-03	2 | 12	DD(6),	3 | 51	DU(23),	1 | 1	DD(1)	GC... ...all 9	7alp... ...all 8
afatinib		chemical drug	afatinib ...all 1	1		-1.667	8.47E-16	2 | 1	DU(1)	2 | 3	DU(2),	2 | 3	IU(3)		
UCP2		transporter	UCP2 ...all 1	1		-1.633	6.82E-13	2 | 7	DD(4),	1 | 1	IU(1)	1 | 1	DD(1)	sirol... ...all 1	PLI... ...all 5
propylthiourac		chemical drug	propylthiouracil ...all 1	1		-1.134	8.83E-13	2 | 1	IU(1)	2 | 3	DU(3)	2 | 1	IU(1)		
sirolimus		chemical drug	sirolimus ...all 1	1		-1.265	3.23E-09	2 | 2	DU(2)	1 | 1	IU(1)	1 | 1	IU(1)		
methimazole		chemical drug	methimazole ...all 1	1		-1.342	2.62E-08	2 | 2	DU(1),	2 | 1	DU(1)	2 | 2	DU(1),		
probenecid		chemical drug	CASP1, DIO2, PANX1, ...all 7	3		0.816	1.23E-06	3 | 5	DU(5)	3 | 77	DU(36),	3 | 7	DU(2),		
HTT		transcription ...	HTT ...all 1	1		-0.447	2.05E-06	1 | 1	IU(1)	1 | 1	DU(1)	2 | 7	DD(2),		sirol... ...all 2



Length (3)

Master Regulator

Specific gene

Participating Regulators

Live Demo

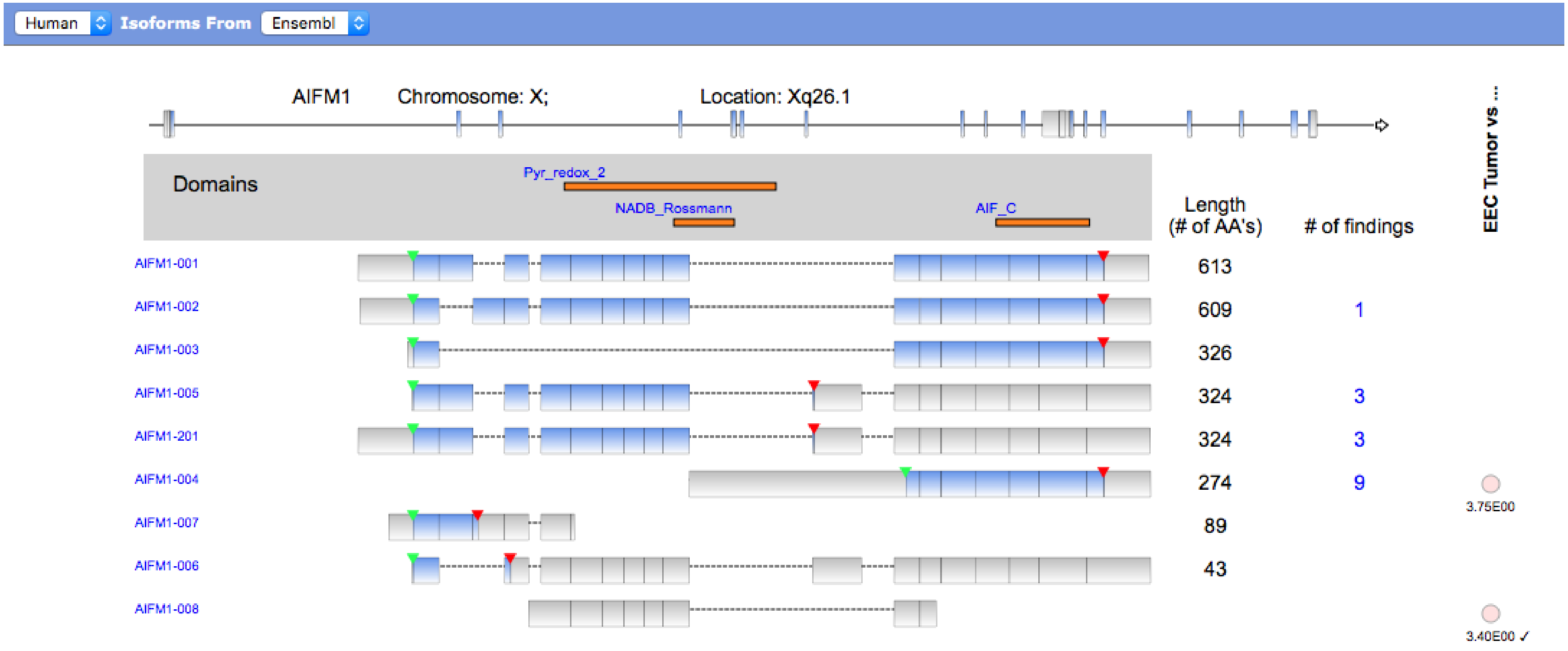
IsoProfiler

IsoProfiler

IsoProfiler displays and enables filtering on transcripts & isoforms in your RNA-seq dataset(s)

Your data must be mapped using **RefSeq**, **Ensembl**, or **UCSC** identifiers. You cannot use gene names or gene-level IDs to map your dataset for IsoProfiler, you must use **transcript** IDs.

Furthermore, for IsoProfiler your dataset must consist of a single source for your dataset-- i.e. only Ensembl, or only RefSeq. **You cannot mix sources**.

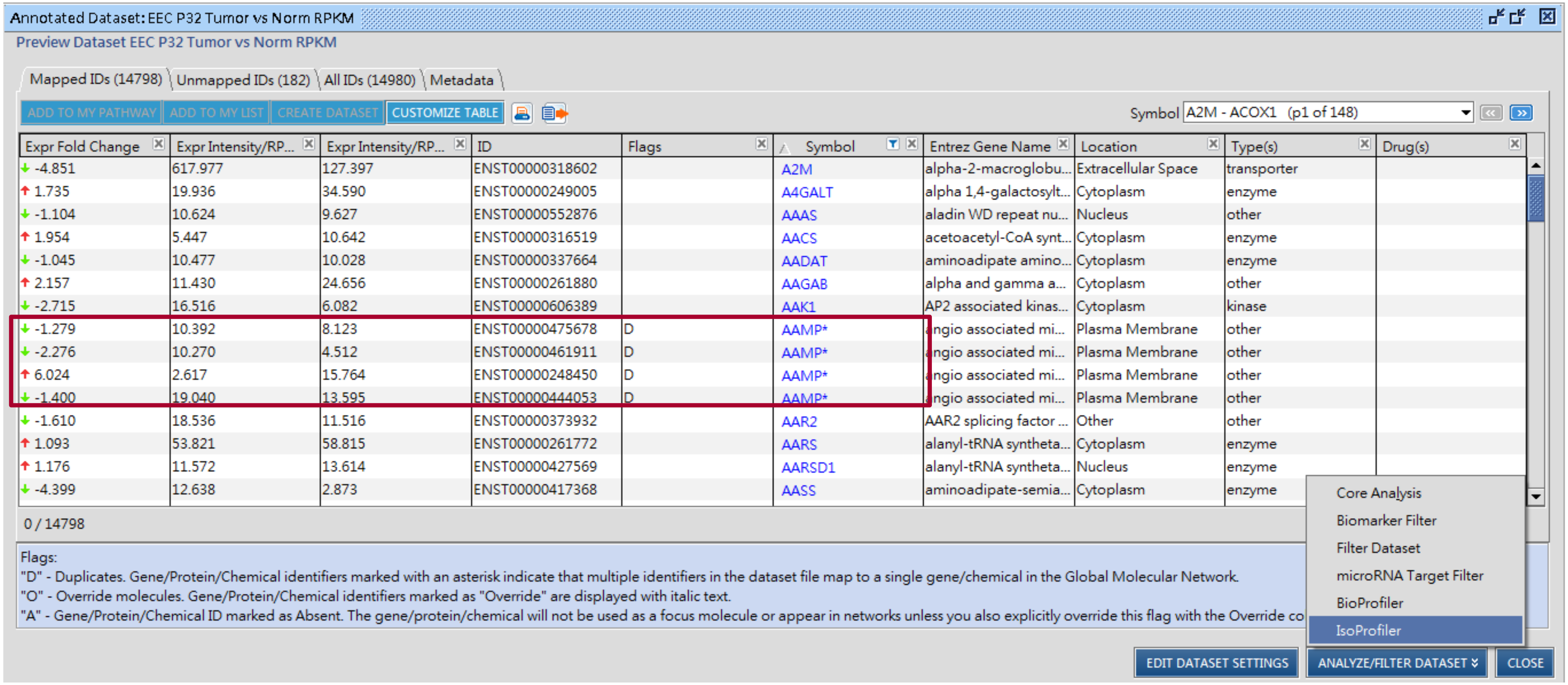


	Length (# of AA's)	# of findings	EEC Tumor vs ...
AIFM1-001	613		
AIFM1-002	609	1	
AIFM1-003	326		
AIFM1-005	324	3	
AIFM1-201	324	3	
AIFM1-004	274	9	3.75E00
AIFM1-007	89		
AIFM1-006	43		
AIFM1-008			3.40E00 ✓

Ensembl ID with isoform viewer in IPA

Dataset Analysis with Isoprofiler

Without Isoprofiler Analysis, different treanscript ID with same gene name can only analysis with the one which has the max expression value.



Expr Fold Change	Expr Intensity/RP...	Expr Intensity/RP...	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
↓ -4.851	617.977	127.397	ENST00000318602		A2M	alpha-2-macroglobu...	Extracellular Space	transporter	
↑ 1.735	19.936	34.590	ENST00000249005		A4GALT	alpha 1,4-galactosylt...	Cytoplasm	enzyme	
↓ -1.104	10.624	9.627	ENST00000552876		AAAS	aladin WD repeat nu...	Nucleus	other	
↑ 1.954	5.447	10.642	ENST00000316519		AACS	acetoacetyl-CoA synt...	Cytoplasm	enzyme	
↓ -1.045	10.477	10.028	ENST00000337664		AADAT	aminoadipate amino...	Cytoplasm	enzyme	
↑ 2.157	11.430	24.656	ENST00000261880		AAGAB	alpha and gamma a...	Cytoplasm	other	
↓ -2.715	16.516	6.082	ENST00000606389		AAK1	AP2 associated kinas...	Cytoplasm	kinase	
↓ -1.279	10.392	8.123	ENST00000475678	D	AAMP*	ngio associated mi...	Plasma Membrane	other	
↓ -2.276	10.270	4.512	ENST00000461911	D	AAMP*	ngio associated mi...	Plasma Membrane	other	
↑ 6.024	2.617	15.764	ENST00000248450	D	AAMP*	ngio associated mi...	Plasma Membrane	other	
↓ -1.400	19.040	13.595	ENST00000444053	D	AAMP*	ngio associated mi...	Plasma Membrane	other	
↓ -1.610	18.536	11.516	ENST00000373932		AAR2	AAR2 splicing factor ...	Other	other	
↑ 1.093	53.821	58.815	ENST00000261772		AARS	alanyl-tRNA syntheta...	Cytoplasm	enzyme	
↑ 1.176	11.572	13.614	ENST00000427569		AARSD1	alanyl-tRNA syntheta...	Nucleus	enzyme	
↓ -4.399	12.638	2.873	ENST00000417368		AASS	aminoadipate-semia...	Cytoplasm	enzyme	

0 / 14798

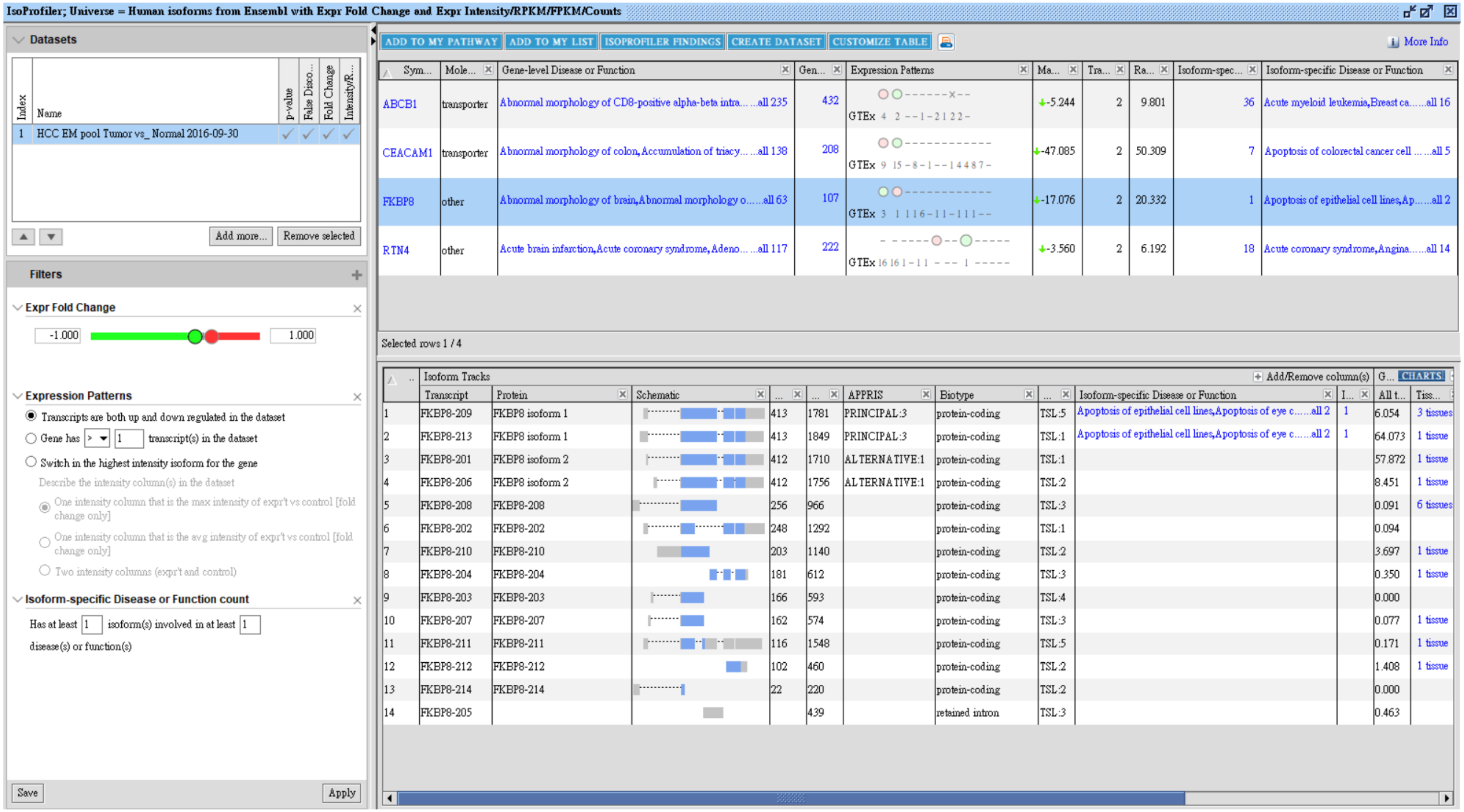
Flags:
"D" - Duplicates. Gene/Protein/Chemical identifiers marked with an asterisk indicate that multiple identifiers in the dataset file map to a single gene/chemical in the Global Molecular Network.
"O" - Override molecules. Gene/Protein/Chemical identifiers marked as "Override" are displayed with italic text.
"A" - Gene/Protein/Chemical ID marked as Absent. The gene/protein/chemical will not be used as a focus molecule or appear in networks unless you also explicitly override this flag with the Override co

IsoProfiler

Once IsoProfiler launches, it will display results such as in this example

Dataset Chooser

Genes and their isoforms from the dataset



IsoProfiler; Universe = Human isoforms from Ensembl with Expr Fold Change and Expr Intensity/RPKM/FPKM/Counts

Datasets

Index	Name	p-value	False Disco...	Fold Change	Intensity/R...
1	HCC EM pool Tumor vs_ Normal 2016-09-30	✓	✓	✓	✓

Filters

Expr Fold Change: -1.000 to 1.000

Expression Patterns

- ● Transcripts are both up and down regulated in the dataset
- ○ Gene has > 1 transcript(s) in the dataset
- ○ Switch in the highest intensity isoform for the gene
  - Describe the intensity column(s) in the dataset
  - ● One intensity column that is the max intensity of expr't vs control [fold change only]
  - ○ One intensity column that is the avg intensity of expr't vs control [fold change only]
  - ○ Two intensity columns (expr't and control)

Isoform-specific Disease or Function count

Has at least 1 isoform(s) involved in at least 1 disease(s) or function(s)

Sym...	Mole...	Gene-level Disease or Function	Gen...	Expression Patterns	Ma...	Tra...	Ra...	Isoform-spec...	Isoform-specific Disease or Function
ABCB1	transporter	Abnormal morphology of CD8-positive alpha-beta intra... ...all 235	432	GTEx 4 2 - - 1 - 2 1 2 2 -	-5.244	2	9.801	36	Acute myeloid leukemia,Breast ca... ...all 16
CEACAM1	transporter	Abnormal morphology of colon, Accumulation of triacy... ...all 138	208	GTEx 9 15 - 8 - 1 - - 1 4 4 8 7 -	-47.085	2	50.309	7	Apoptosis of colorectal cancer cell ... ...all 5
FKBP8	other	Abnormal morphology of brain,Abnormal morphology o... ...all 63	107	GTEx 3 1 1 1 6 - 1 1 - 1 1 1 - -	-17.076	2	20.332	1	Apoptosis of epithelial cell lines,Ap... ...all 2
RTN4	other	Acute brain infarction,Acute coronary syndrome, Adeno... ...all 117	222	GTEx 16 16 1 - 1 1 - - - 1 - - - - -	-3.560	2	6.192	18	Acute coronary syndrome,Angina... ...all 14

Selected rows 1 / 4

Isoform Tracks

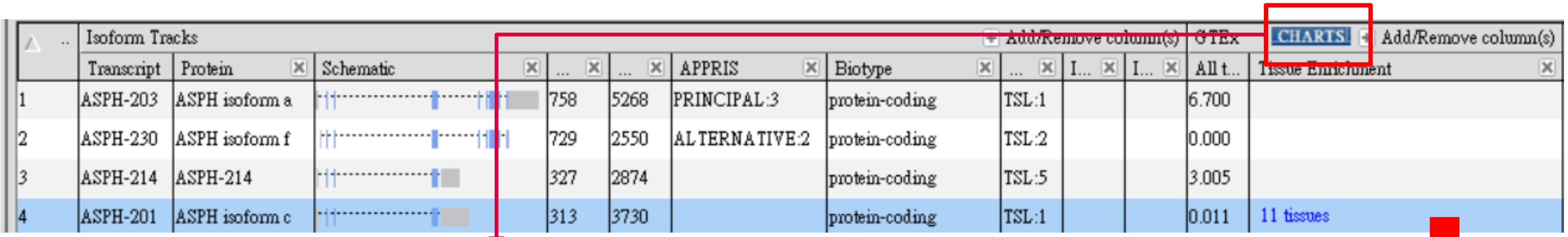
	Transcript	Protein	Schematic	...	...	APPRIS	Biotype	...	Isoform-specific Disease or Function	I...	All t...	Tiss...
1	FKBP8-209	FKBP8 isoform 1		413	1781	PRINCIPAL:3	protein-coding	TSL:5	Apoptosis of epithelial cell lines,Apoptosis of eye c... ...all 2	1	6.054	3 tissues
2	FKBP8-213	FKBP8 isoform 1		413	1849	PRINCIPAL:3	protein-coding	TSL:1	Apoptosis of epithelial cell lines,Apoptosis of eye c... ...all 2	1	64.073	1 tissue
3	FKBP8-201	FKBP8 isoform 2		412	1710	ALTERNATIVE:1	protein-coding	TSL:1			57.872	1 tissue
4	FKBP8-206	FKBP8 isoform 2		412	1756	ALTERNATIVE:1	protein-coding	TSL:2			8.451	1 tissue
5	FKBP8-208	FKBP8-208		256	966		protein-coding	TSL:3			0.091	6 tissues
6	FKBP8-202	FKBP8-202		248	1292		protein-coding	TSL:1			0.094	
7	FKBP8-210	FKBP8-210		203	1140		protein-coding	TSL:2			3.697	1 tissue
8	FKBP8-204	FKBP8-204		181	612		protein-coding	TSL:3			0.350	1 tissue
9	FKBP8-203	FKBP8-203		166	593		protein-coding	TSL:4			0.000	
10	FKBP8-207	FKBP8-207		162	574		protein-coding	TSL:3			0.077	1 tissue
11	FKBP8-211	FKBP8-211		116	1548		protein-coding	TSL:5			0.171	1 tissue
12	FKBP8-212	FKBP8-212		102	460		protein-coding	TSL:2			1.408	1 tissue
13	FKBP8-214	FKBP8-214		22	220		protein-coding	TSL:2			0.000	
14	FKBP8-205				439		retained intron	TSL:3			0.463	

Isoform filters

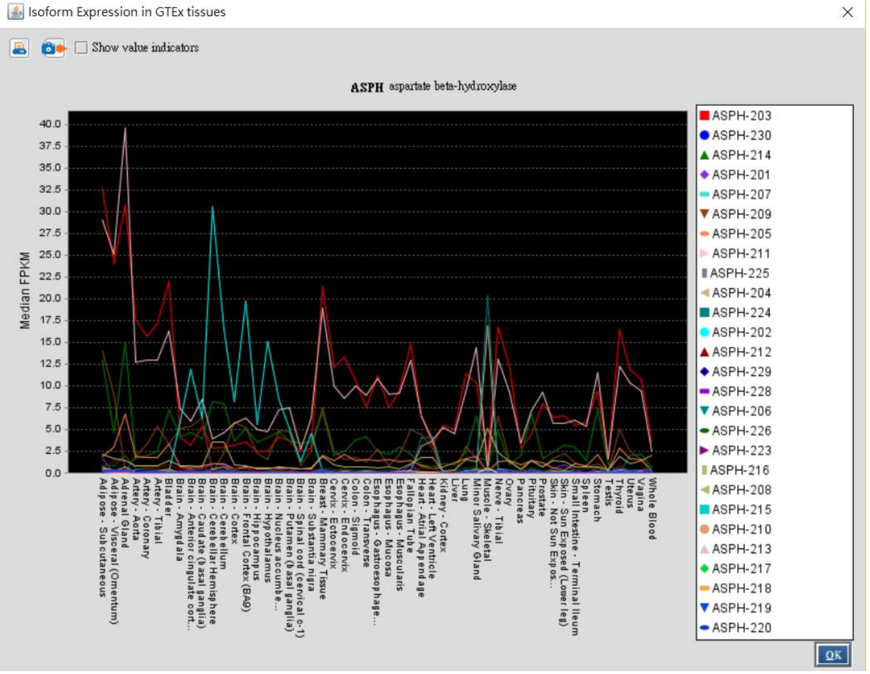
Isoform details on the selected gene

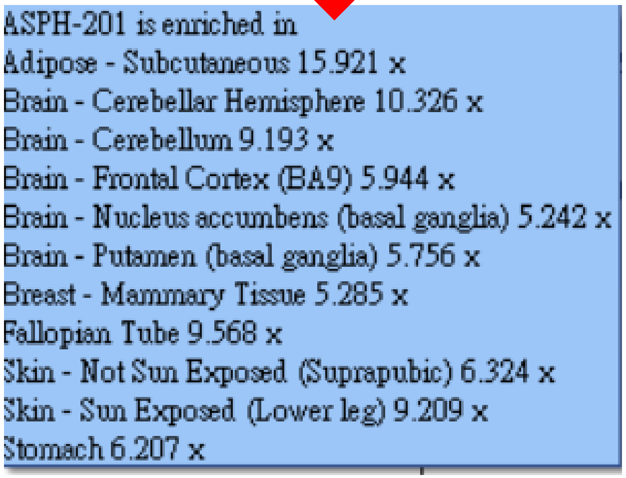
IsoProfiler with **GTEx Tissue Expression**

If your dataset is based on human expression data, additional functionality appears in IsoProfiler to help you explore tissue expression information from the **GTEx consortium**, which profiled **51 tissues** from multiple human tissue donors by RNA-seq.



Isoform Tracks								Add/Remove column(s)			GTEx	CHARTS Add/Remove column(s)
	Transcript	Protein	Schematic	...	...	APPRIS	Biotype	...	I...	I...	All t...	Tissue Enrichment
1	ASPH-203	ASPH isoform a		758	5268	PRINCIPAL:3	protein-coding	TSL:1			6.700	
2	ASPH-230	ASPH isoform f		729	2550	ALTERNATIVE:2	protein-coding	TSL:2			0.000	
3	ASPH-214	ASPH-214		327	2874		protein-coding	TSL:5			3.005	
4	ASPH-201	ASPH isoform c		313	3730		protein-coding	TSL:1			0.011	11 tissues





ASPH-201 is enriched in
Adipose - Subcutaneous 15.921 x
Brain - Cerebellar Hemisphere 10.326 x
Brain - Cerebellum 9.193 x
Brain - Frontal Cortex (BA9) 5.944 x
Brain - Nucleus accumbens (basal ganglia) 5.242 x
Brain - Putamen (basal ganglia) 5.756 x
Breast - Mammary Tissue 5.285 x
Fallopian Tube 9.568 x
Skin - Not Sun Exposed (Suprapubic) 6.324 x
Skin - Sun Exposed (Lower leg) 9.209 x
Stomach 6.207 x

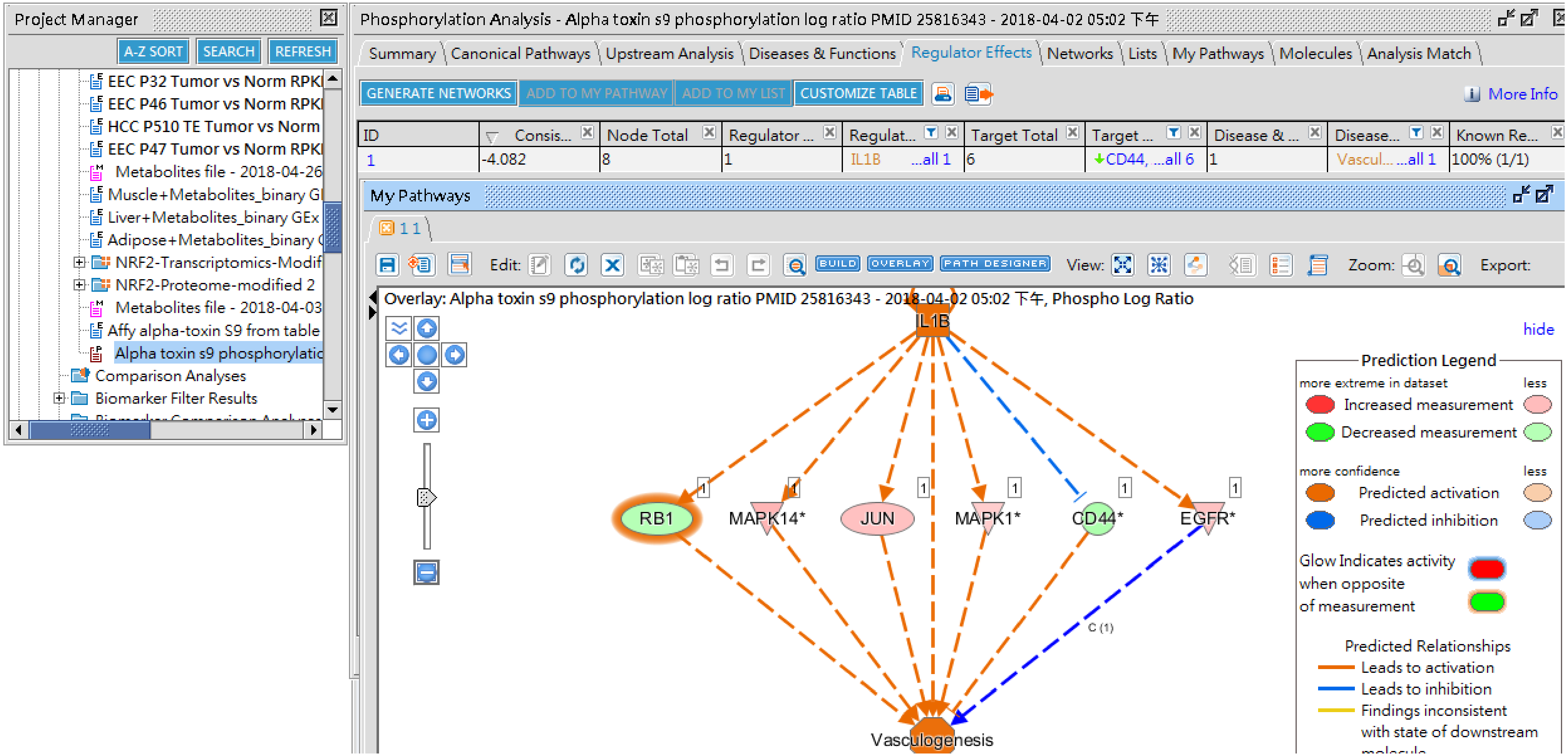
The GTEx consortium has performed over 9,800 paired-end RNA-Seq experiments across 51 human tissues

Live Demo

PhosphoProteomics

PhosphoProteomics Analysis

Find out how to understand your Phosphoproteomics Analysis and about the multiple ways of relating the molecules in your dataset to the body of information in the Ingenuity Knowledge Base.



Project Manager

- EEC P32 Tumor vs Norm RPKI
- EEC P46 Tumor vs Norm RPKI
- HCC P510 TE Tumor vs Norm
- EEC P47 Tumor vs Norm RPKI
- Metabolites file - 2018-04-26
- Muscle+Metabolites_binary GI
- Liver+Metabolites_binary GEx
- Adipose+Metabolites_binary (
- NRF2-Transcriptomics-Modif
- NRF2-Proteome-modified 2
- Metabolites file - 2018-04-03
- Affy alpha-toxin S9 from table
- Alpha toxin s9 phosphorylatio
- Comparison Analyses
- Biomarker Filter Results

Phosphorylation Analysis - Alpha toxin s9 phosphorylation log ratio PMID 25816343 - 2018-04-02 05:02 下午

ID	Consis...	Node Total	Regulator ...	Regulat...	Target Total	Target ...	Disease & ...	Disease...	Known Re...
1	-4.082	8	1	IL1B ...all 1	6	CD44, ...all 6	1	Vascul... ...all 1	100% (1/1)

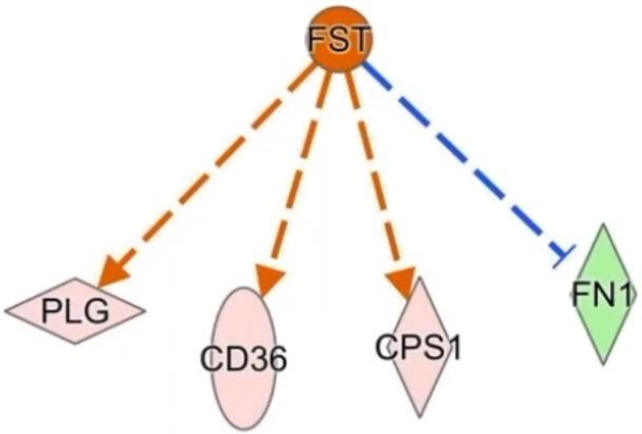
My Pathways

Overlay: Alpha toxin s9 phosphorylation log ratio PMID 25816343 - 2018-04-02 05:02 下午, Phospho Log Ratio

PhosphoProteomics Analysis

Gene expression data:

FST causes the up-or-down-regulation of target genes

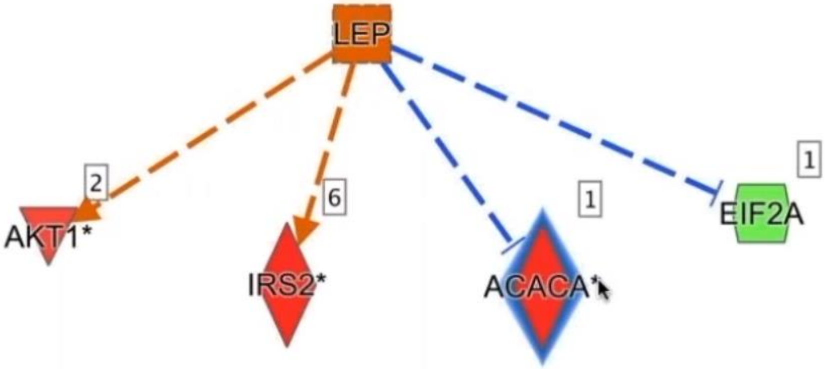


PLG, CD36, CPS1 are *up-regulated* by *activated* PST

FN1 is *down-regulated* by *activated* PST

Phosphorylation data:

LEP causes the up-or-down phosphorylation of target proteins



AKT1, IRS2 are *activated* by *increased* phosphorylation from *activated* LEP

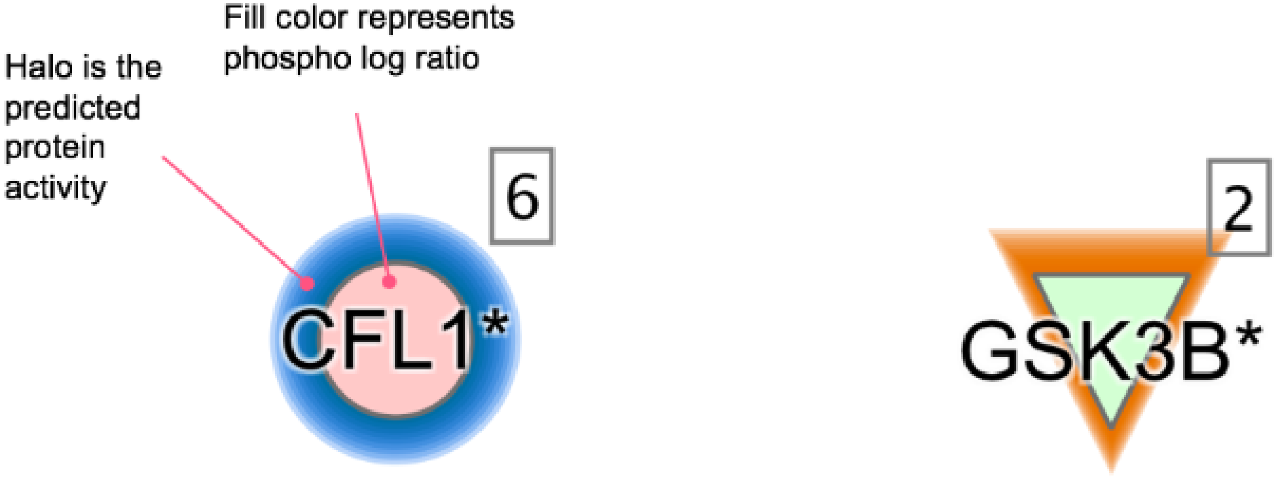
EIF2A's activity is *inhibited* by *decreased* phosphorylation from *activated* LEP

ACACA has *increased* phosphorylation from *activated* LEP

The blue halo indicates that phosphorylation cause *inhibition* of ACACA's activity

PhosphoProteomics Analysis

Halos indicate the protein's activity when it is *opposite* of the direction of phosphorylation



Fill color represents phospho log ratio

Halo is the predicted protein activity

CFL1 has *increased* phosphorylation in dataset but prediction of *decreased* protein activity

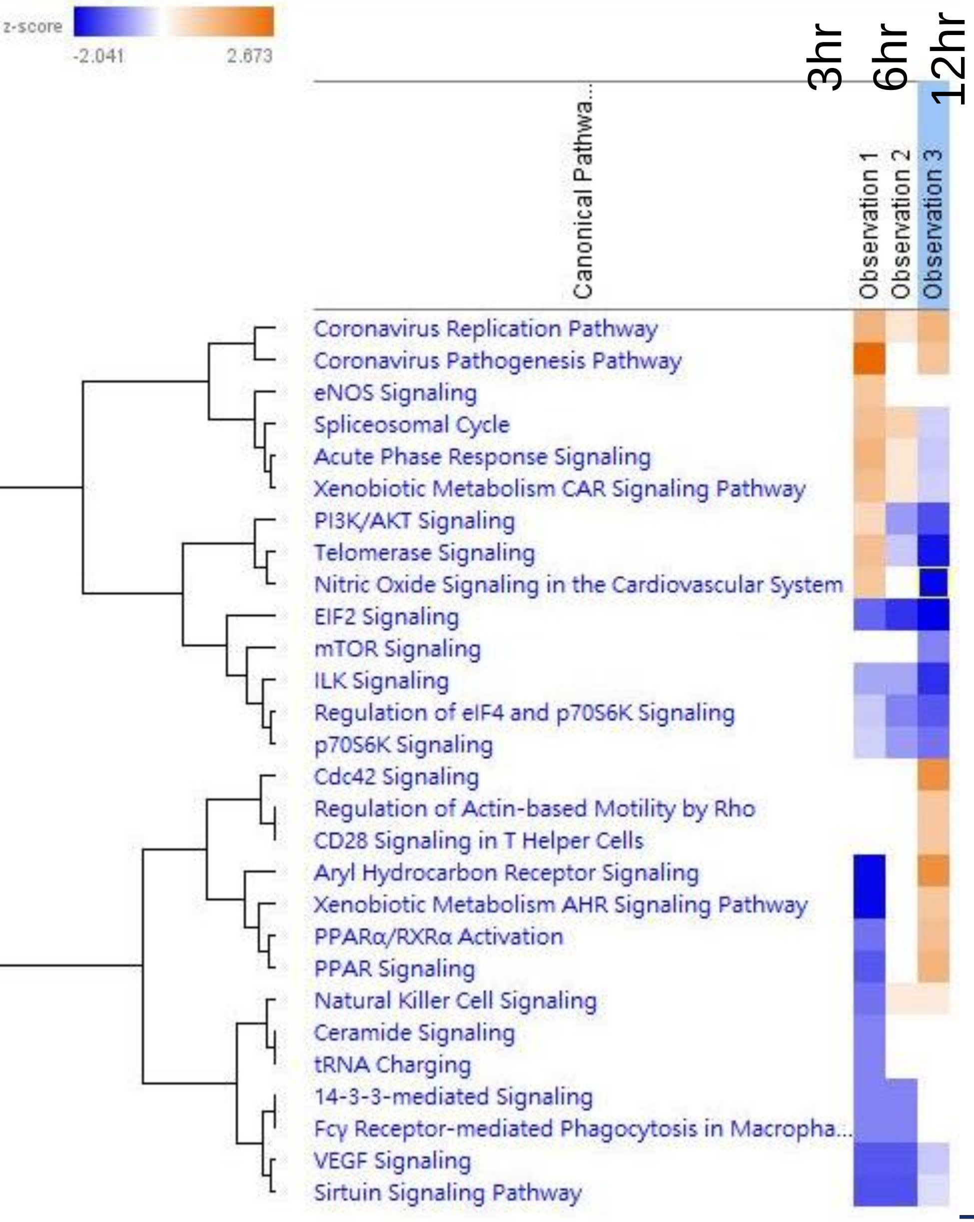
GSK3B has *decreased* phosphorylation in dataset but prediction of *increased* protein activity

Find out how to understand your Phosphoproteomics Analysis and about the multiple ways of relating the molecules in your dataset to the body of information in the Ingenuity Knowledge Base.

Live Demo

Case Study

Case Study of ITRAq data



Comparison Analysis of Canonical Pathways

Coronavirus Pathway activated

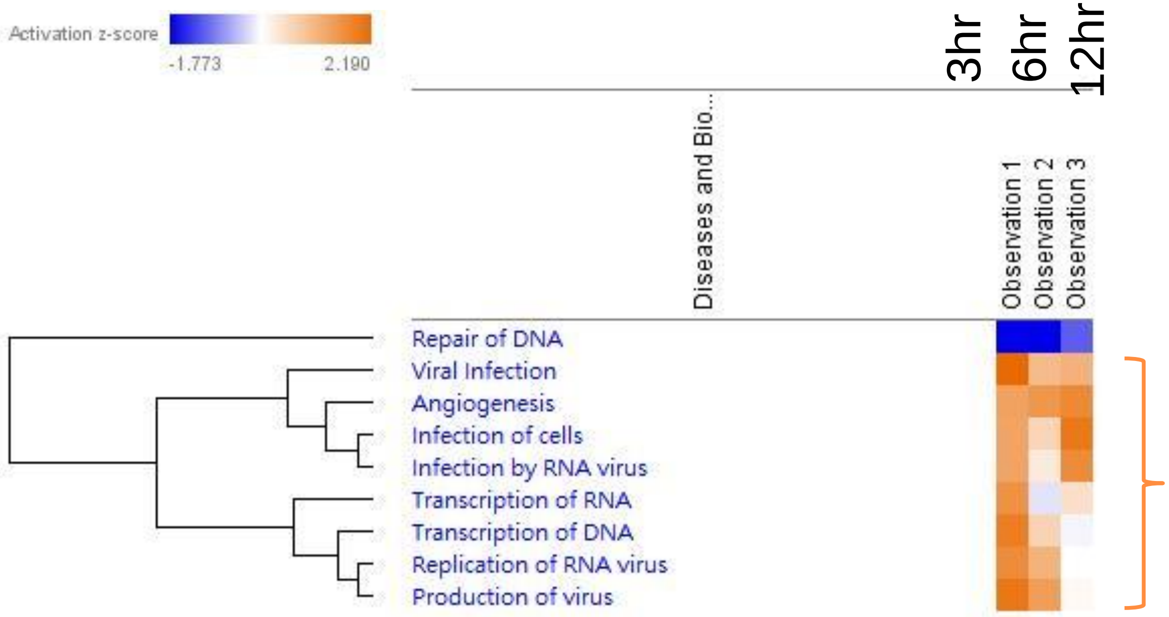
Cardiovascular System inhibited

PPAR Signaling activated

Case Study of ITRAq data

Comparison Analysis of Disease and Function

| Z-score | > 1.5



Virus function activated

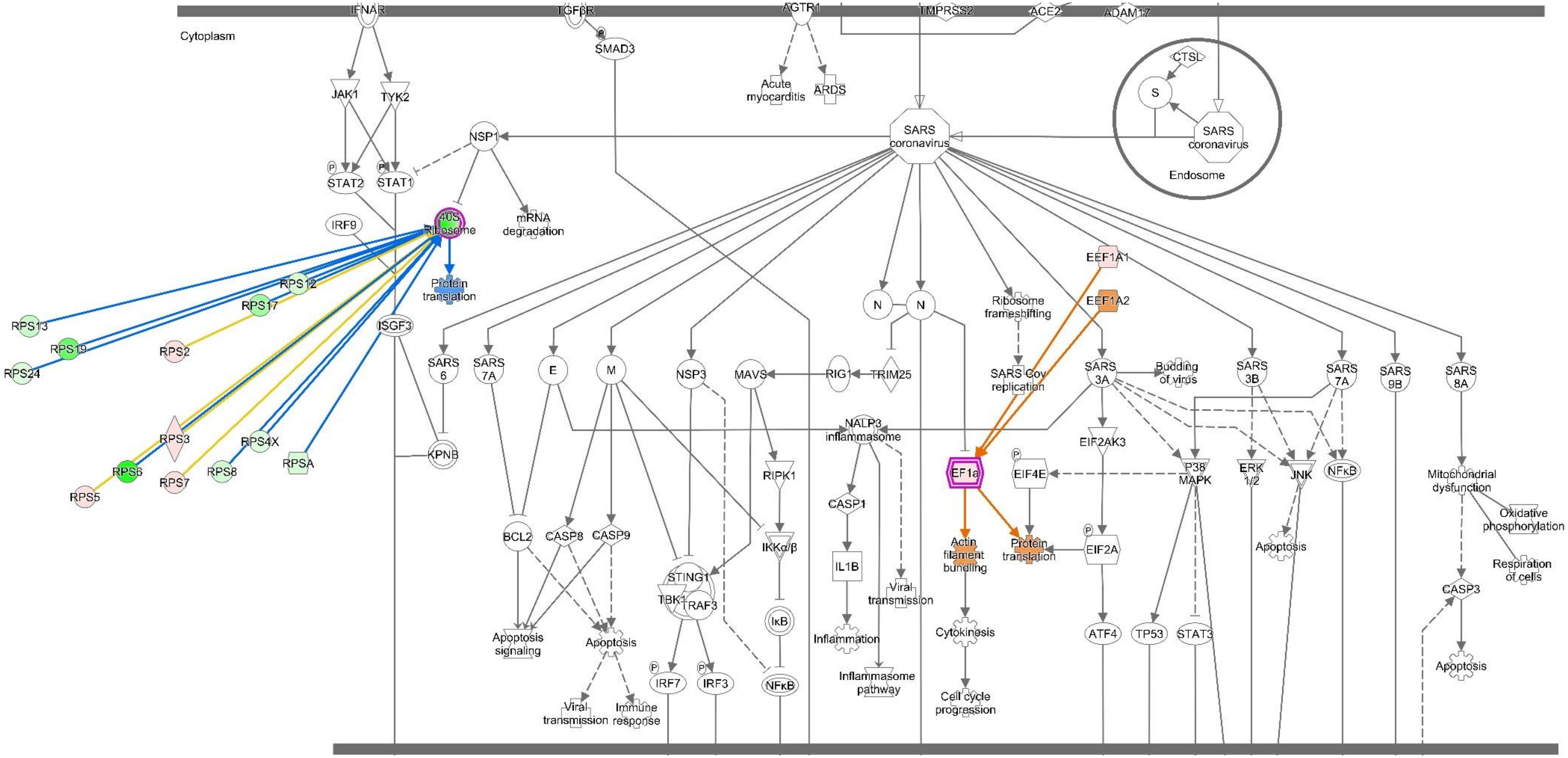
Case Study of ITRAq data

Coronavirus Pathogenesis Pathway

Z-score = 2.67

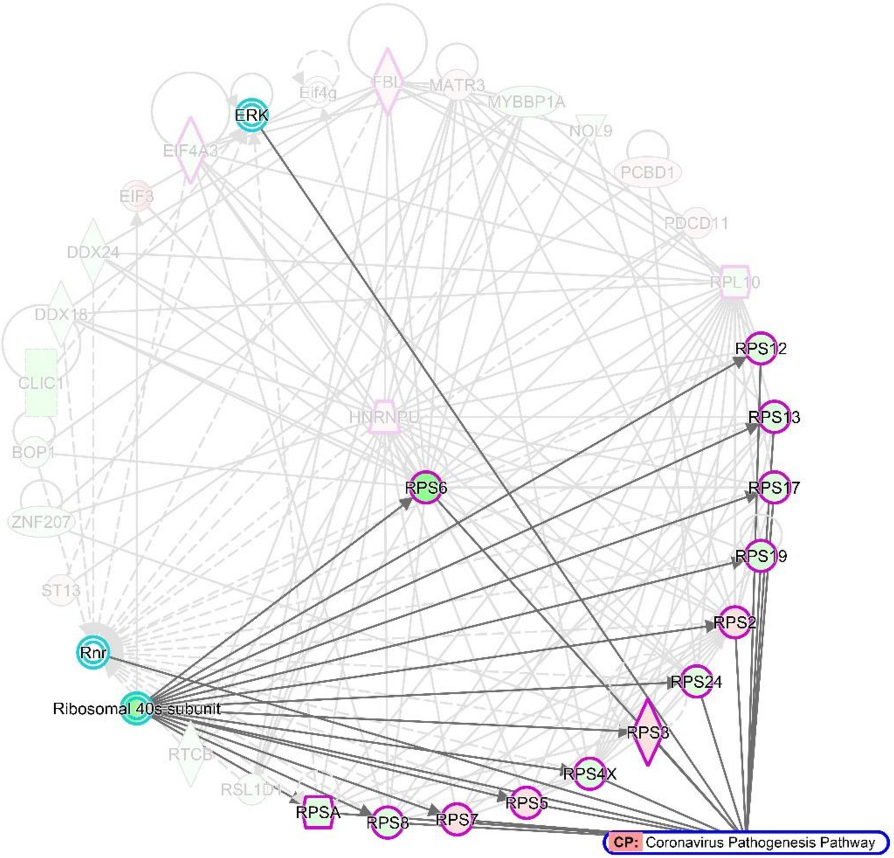
-log P-value = 8.5

Molecules = 15

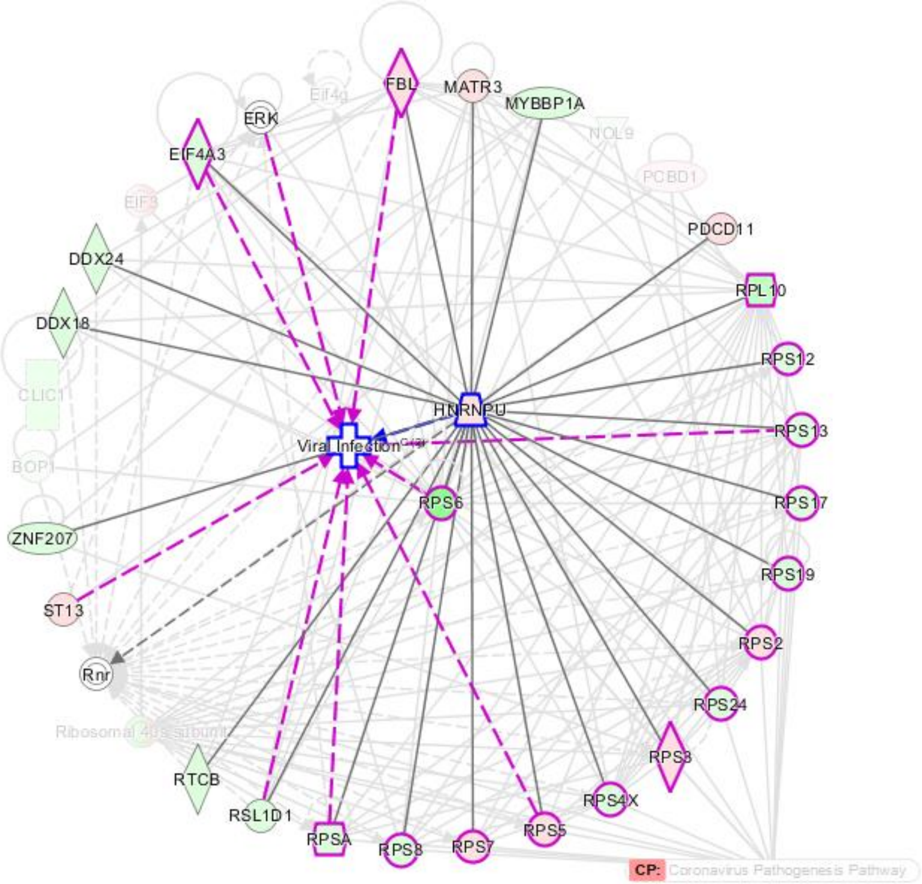


Case Study of ITRAq data

Key:
- 40s Ribosome
- Coronavirus Pathogenesis Pathway

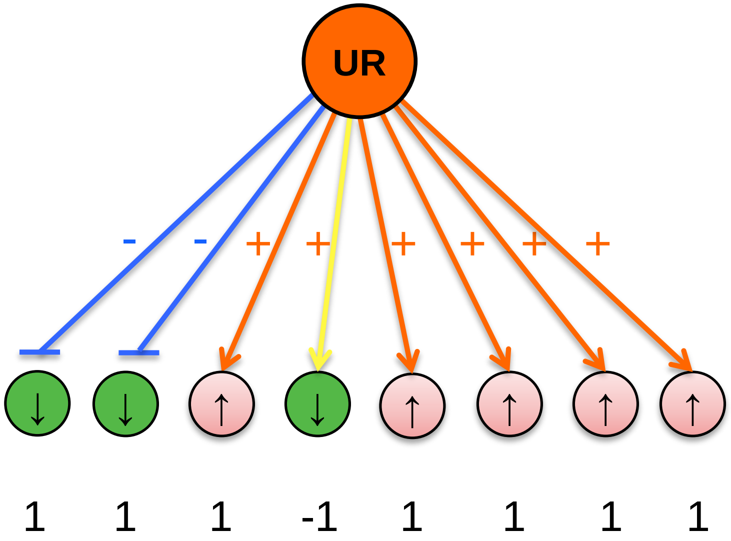


Key:
- HNRNPU
- Viral Infection



Q&A

Predicting upstream regulators of a dataset



← Every possible TF & Upstream Regulator in the
Ingenuity Knowledge Base is analyzed

← Literature-based effect TF/UR has on downstream genes

← Differential Gene Expression (Uploaded Data)

← Predicted activation state of TF/UR:
1 = Consistent with activation of UR
-1 = Consistent with inhibition of UR

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}}$$

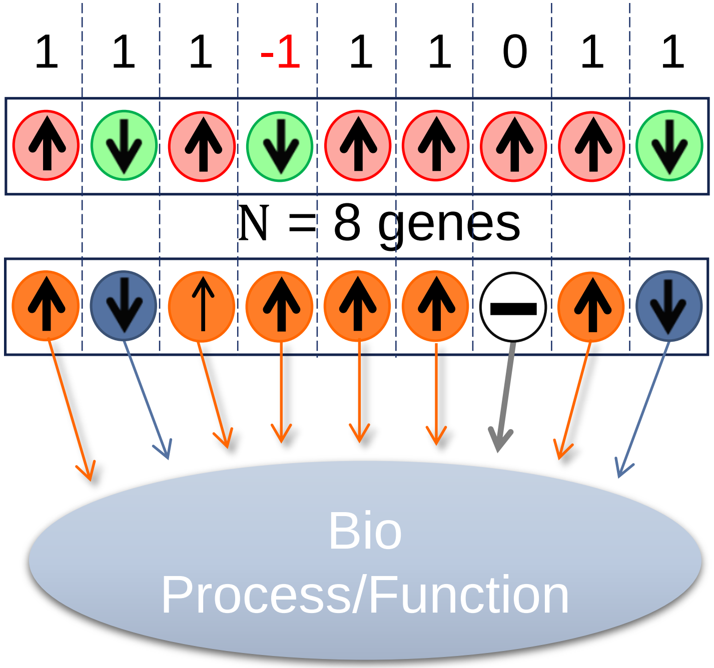
$=(7-1)/\sqrt{8} = 2.12$ (=predicted activation)

- z-score is a statistical measure of the match between expected relationship direction and observed gene expression
- z-score > 2 or < -2 is considered significant

Note that the actual z-score is weighted by the underlying findings, the relationship bias, and dataset bias

Downstream Effect Activation z–score

Statistical measure of correlation between the relationship direction and resulting gene expression



Differential gene expression
(Uploaded Data)

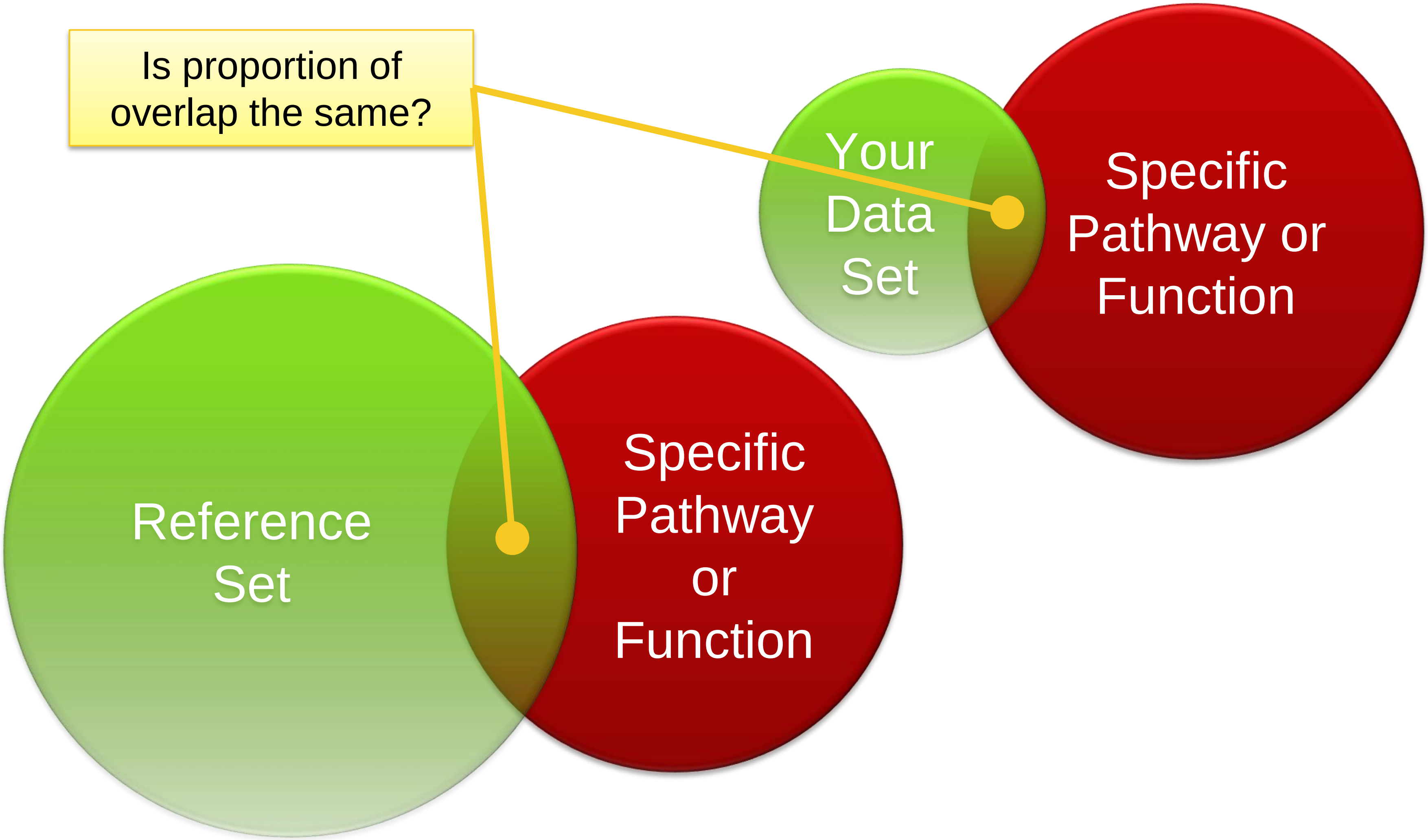
Effect genes have on a process or function
(Literature)

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}}$$

z-score > 2 or < -2 is considered significant

Actual z-score *can* be weighted by relationship types, relationship bias, data bias

Determining Significance of Your Data to IPA



Is proportion of overlap the same?

Important note: Statistics in Biology

The Fisher's Exact Test

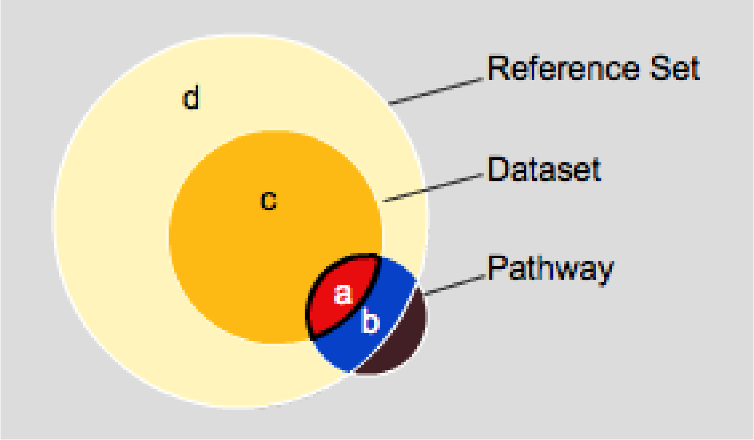
Given a list of differentially expressed genes in a dataset, what is the probability that the overlap with the set of genes on a particular pathway is by random chance?

The null hypothesis is that the association occurs purely by chance.

The Fisher's Exact Test is a way to test for significant associations

The test looks at the **number** of genes

a. That match between pathway and dataset
b. That are in pathway but did not match dataset
c. That are in dataset but did not match pathway
d. That were possible to assay in the experiment but are not in the pathway or dataset (this is usually called the "reference set" and is ~the set of all genes on the array platform)



The calculation returns a **p-value:**
From 0-1, where values <0.05 are generally considered significant)

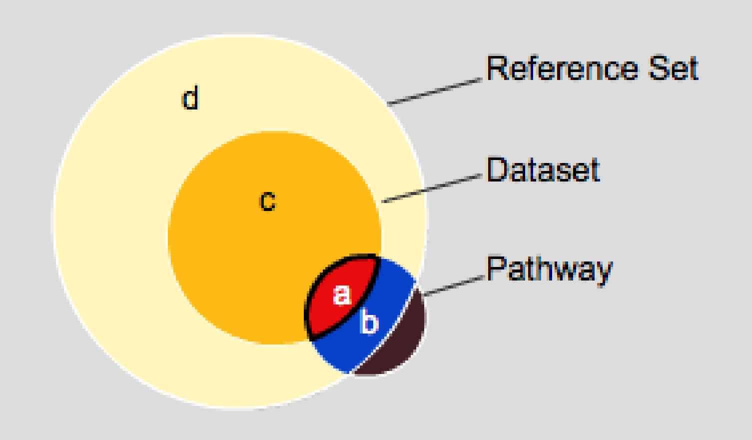
Statistics in Biology: Fisher's Exact, continued

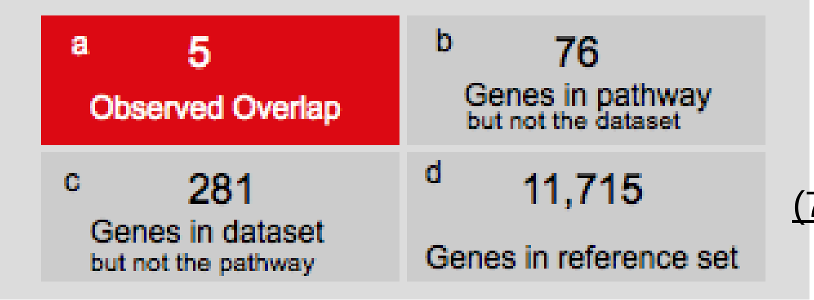
If you had this situation:

- Dataset (significantly differentially expressed) of 286 genes
- Pathway of 81 genes
- Where 5 of the dataset genes overlap those in the pathway
- And the platform measured about 12,000 genes

What is the significance of that overlap?

$$\text{p-value} = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{(a+b+c+d)!a!b!c!d!}$$





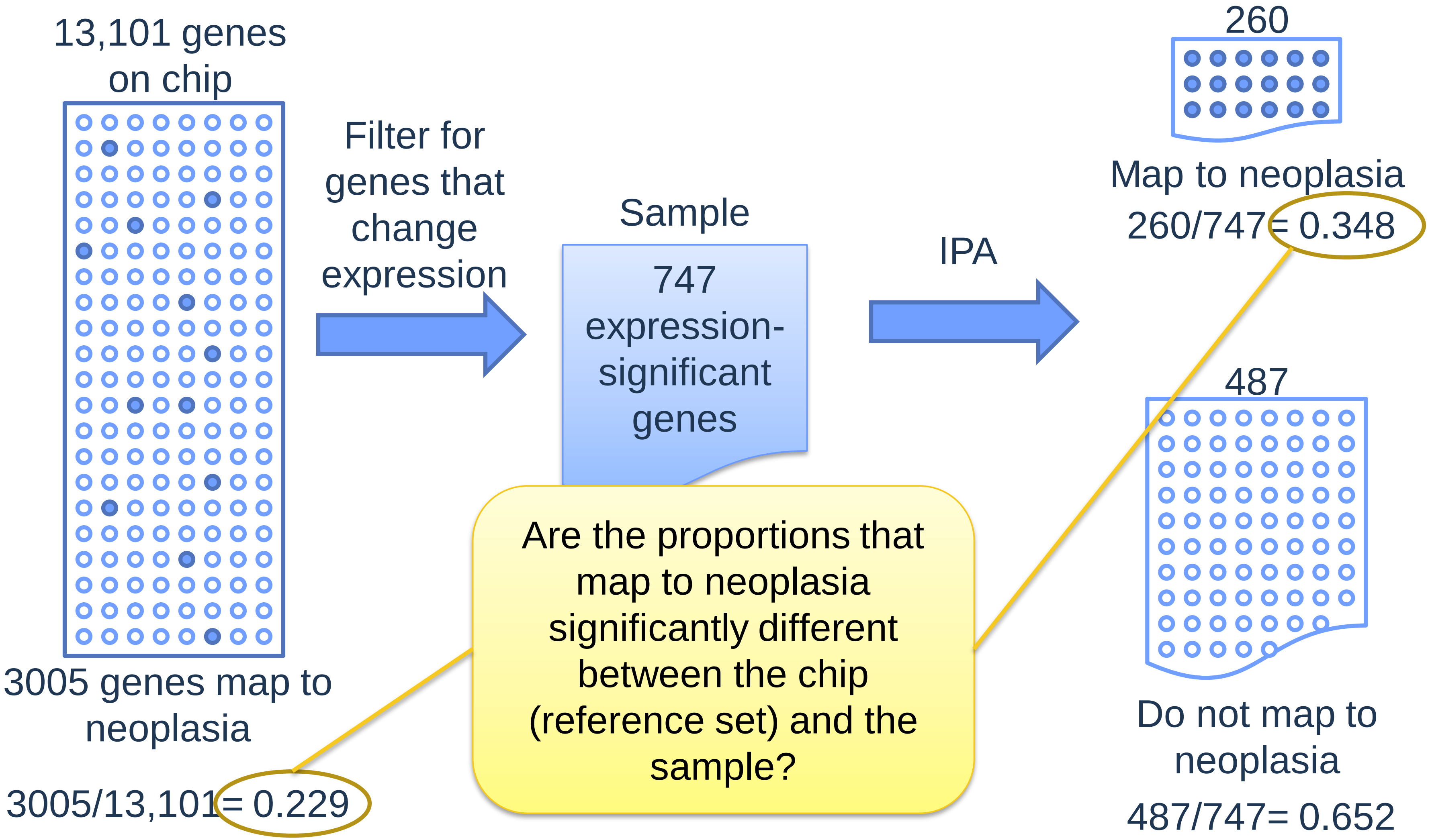
a 5 Observed Overlap	b 76 Genes in pathway but not the dataset
c 281 Genes in dataset but not the pathway	d 11,715 Genes in reference set

$$p = \frac{(5+76)!\ (281+11715)!\ (5+281)!\ (76+11715)!}{(5+76+281+11715)!\ 5!\ 76!\ 281!\ 11715!}$$

$$=0.043$$

Note: "!" is the factorial operator, where for example 3! = 3 x 2 x 1 = 6

Mapping Colorectal Cancer Expression Data to the Function “Neoplasia”



13,101 genes on chip

Filter for genes that change expression

Sample

747 expression-significant genes

IPA

260

Map to neoplasia

260/747= 0.348

487

Do not map to neoplasia

487/747= 0.652

3005 genes map to neoplasia

3005/13,101= 0.229

Are the proportions that map to neoplasia significantly different between the chip (reference set) and the sample?

Calculating the Fisher’s Exact Test

- For IPA, a 2x2 contingency table is created based on the total population, the sample, and how many genes map to the function/pathway. This table is used to calculate the Fisher’s exact test.

	Neoplasia	Not Neoplasia	
In Sample	k	n - k	n
Not in Sample	m - k	N + k - n - m	N - n
	m	N - m	N

m= Total that map to function/pathway
N= Total
k= Number that map to function/pathway in sample
n= Total sample

What Does the p-Value Mean?

- The smaller the p-value, the less likely an observed proportion of genes mapping to a function or pathway is a result of chance. We then infer that there is a biological effect.
  - A p-value of 0.05 indicates that you should expect to observe the gene proportion mapping to a function or pathway by chance in one out of 20 (5 out of 100) repeated experiments of the same size

What is the Fisher’s Exact Test

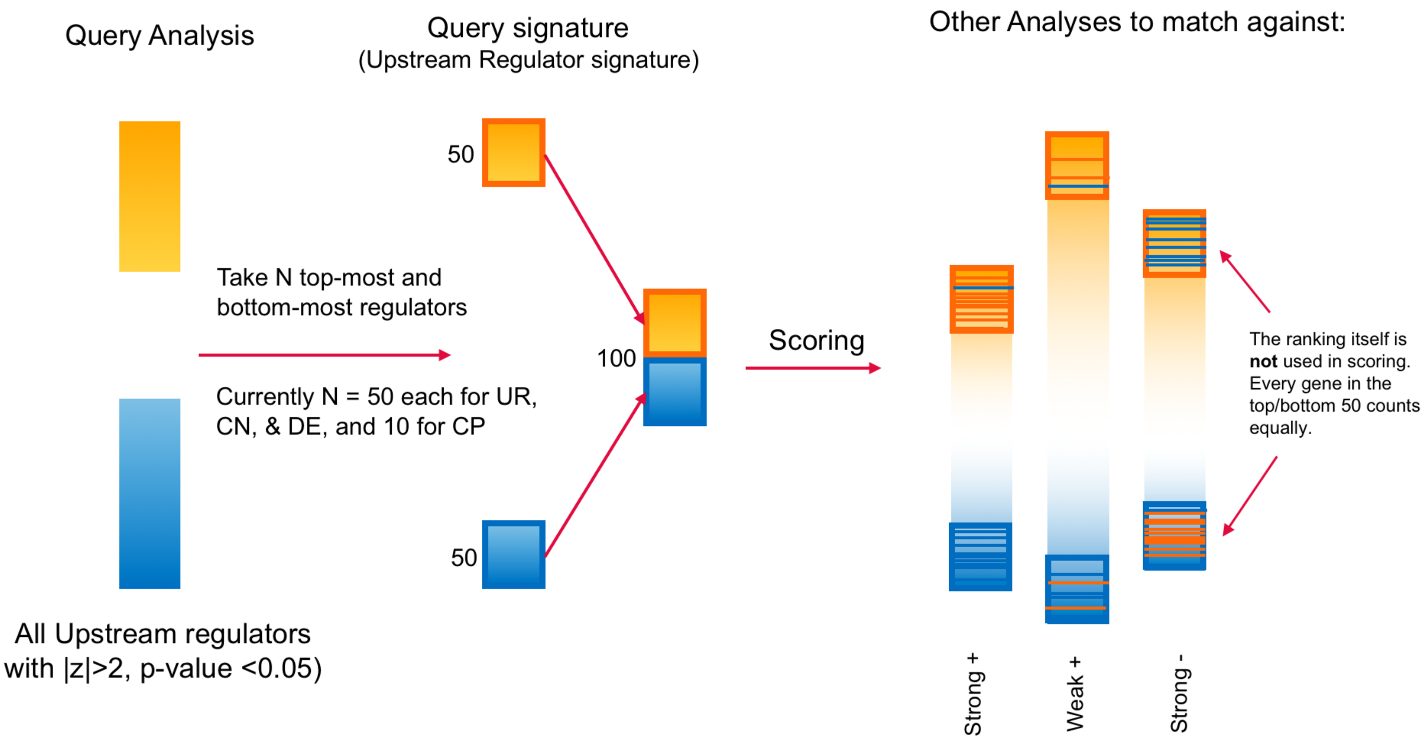
- The Fisher’s exact test is a statistical test, similar to the chi-square test, used for categorical data that result from classifying objects in two different ways
- It is used to examine the significance of the association (contingency) between the two kinds of classification
  - In IPA, the two categories are the uploaded dataset and a particular pathway or function
  - A Fisher’s exact test is used instead of the chi-square test because the number of genes that map to a function or pathway can be less than five and would cause the chi-square test to be inaccurate

How Analysis Match z-score are calculated for your analysis

How signatures are created and compared

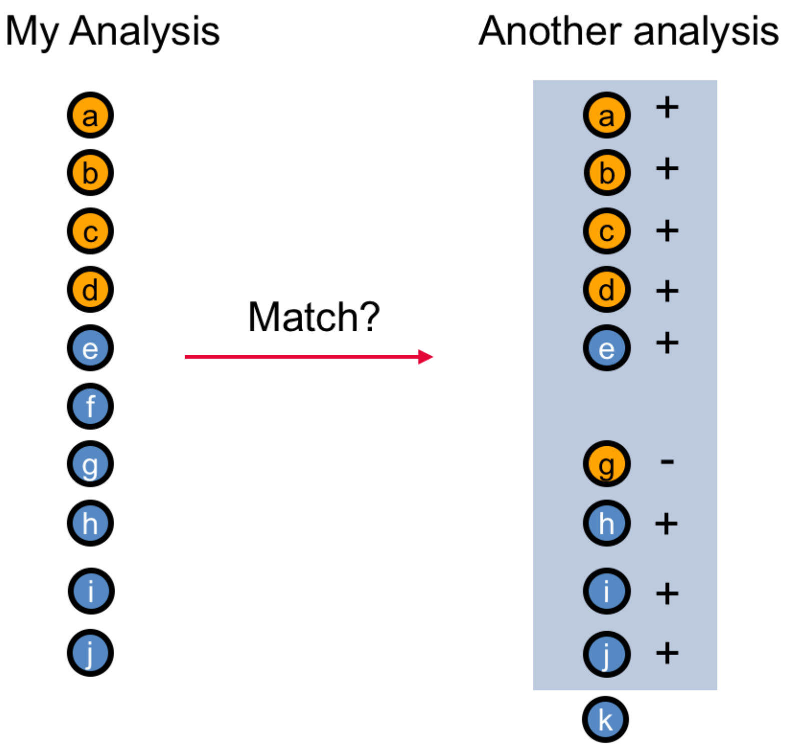
Canonical Pathways (up to 20 pathways)
Upstream Regulators (up to 100 regulators)
Causal Networks (up to 100 master regulators)
Diseases & Functions (up to 100 diseases or functions)

Example



Analysis Match – explanation of z-score

How signatures are created and compared



Query
Upstream Regulator
signature

Scoring against
Upstream Regulator
signature from
another analysis

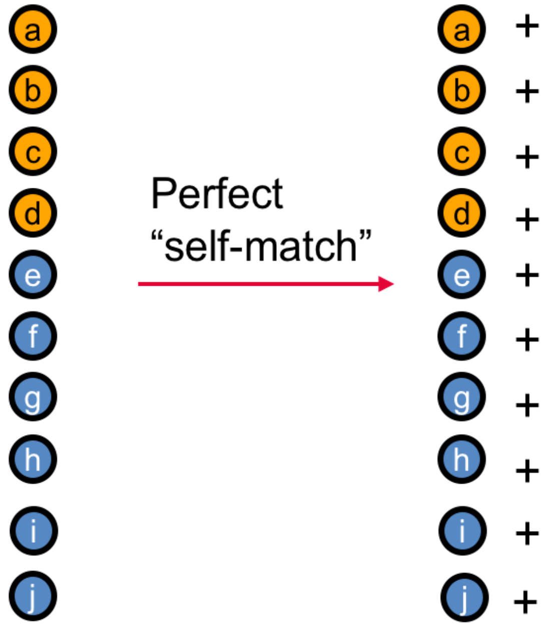
$$Z = \frac{\text{matches - mismatches}}{\text{Square root of all matches}}$$

- z-score is a measure of the match between two patterns
- Assumes the pattern is created from two sets of entities where the sign of the matching entities is random

$= (8-1)/\sqrt{9} = 2.33$ (raw z-score)

Yes, it matches (because $z>2$)

Steps for normalizing the z-score for a match percentage



My Analysis

My Analysis

Perfect
“self-match”

Query
Upstream Regulator
signature

Query
Upstream Regulator
signature

First, find out the **max** possible z-score for a perfect match for this particular analysis:
= (10-0)/√10 = 3.16 (It’s really just equal to √N)

Then divide the **actual** z-score for the matching analysis by the calculated **max**.

In this example:
Normalized z-score for the matching analysis is 2.33/3.16 = 74%

How are Overall scores calculated in Analysis match

For z-score

- Simply take average of percentages for all four entities

CP (z-score)	UR (z-score)	CN (z-score)	DE (z-score)	z-score overall score
50.00	60.91	53.85	40.49	51.31

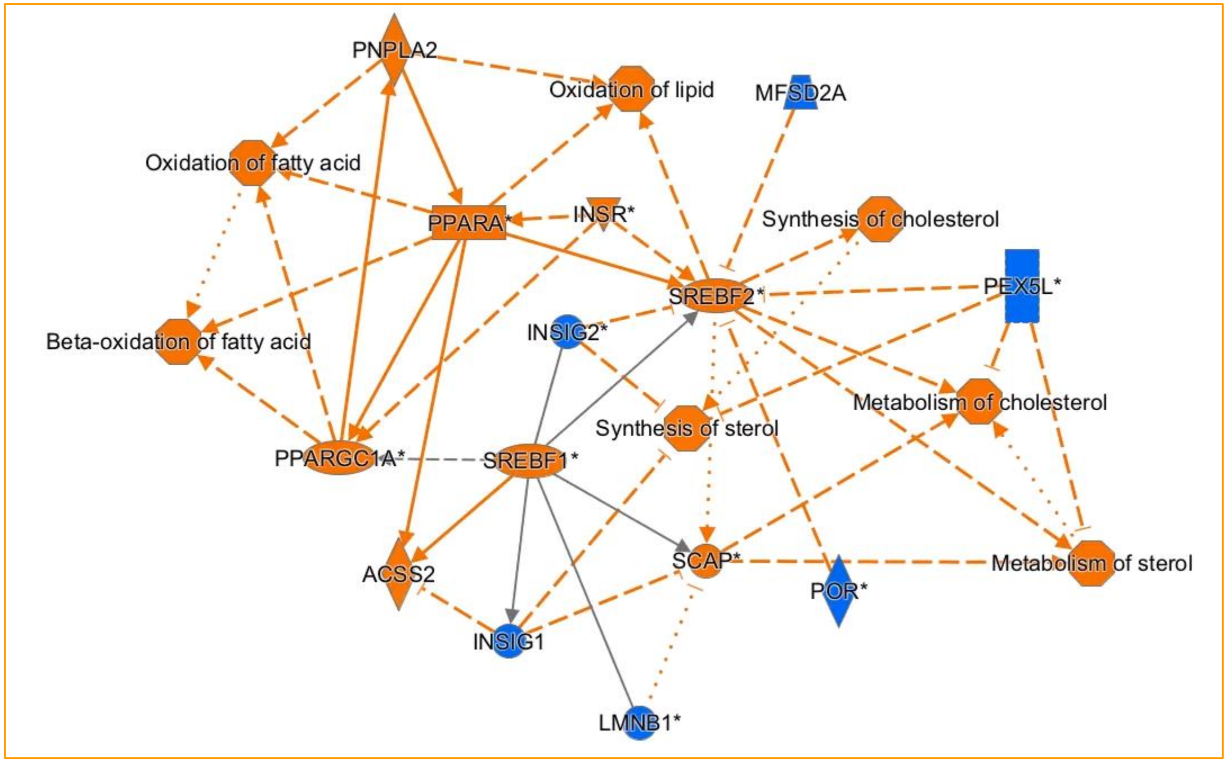
Average of the four
percentages

For p-value

- P-value percentage for entities are not reported
- Take the –log 10 of each p-value (if –log 10 of p-value is >50, then just set it to 50)
- Calculate % vs. the maximum possible p-value (self vs. self match)
- Take average of percentages for all four entities

Graphical Summary

Graphical Summary結果:
將資料集最相關的生物主題以網路圖像呈現
(canonical pathways, upstream regulators, causal network master regulators, diseases, and biological functions)

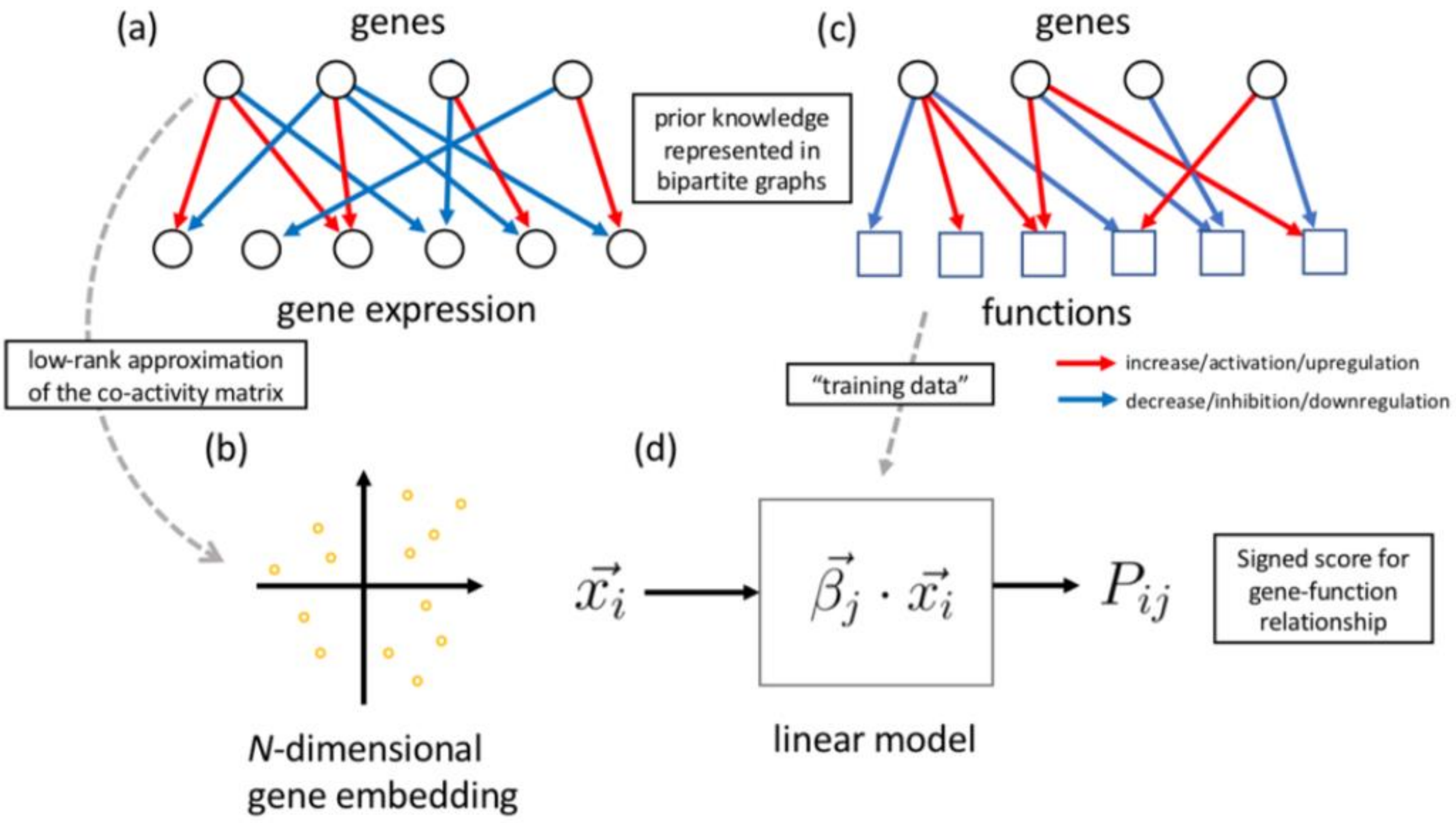


Criteria for selection

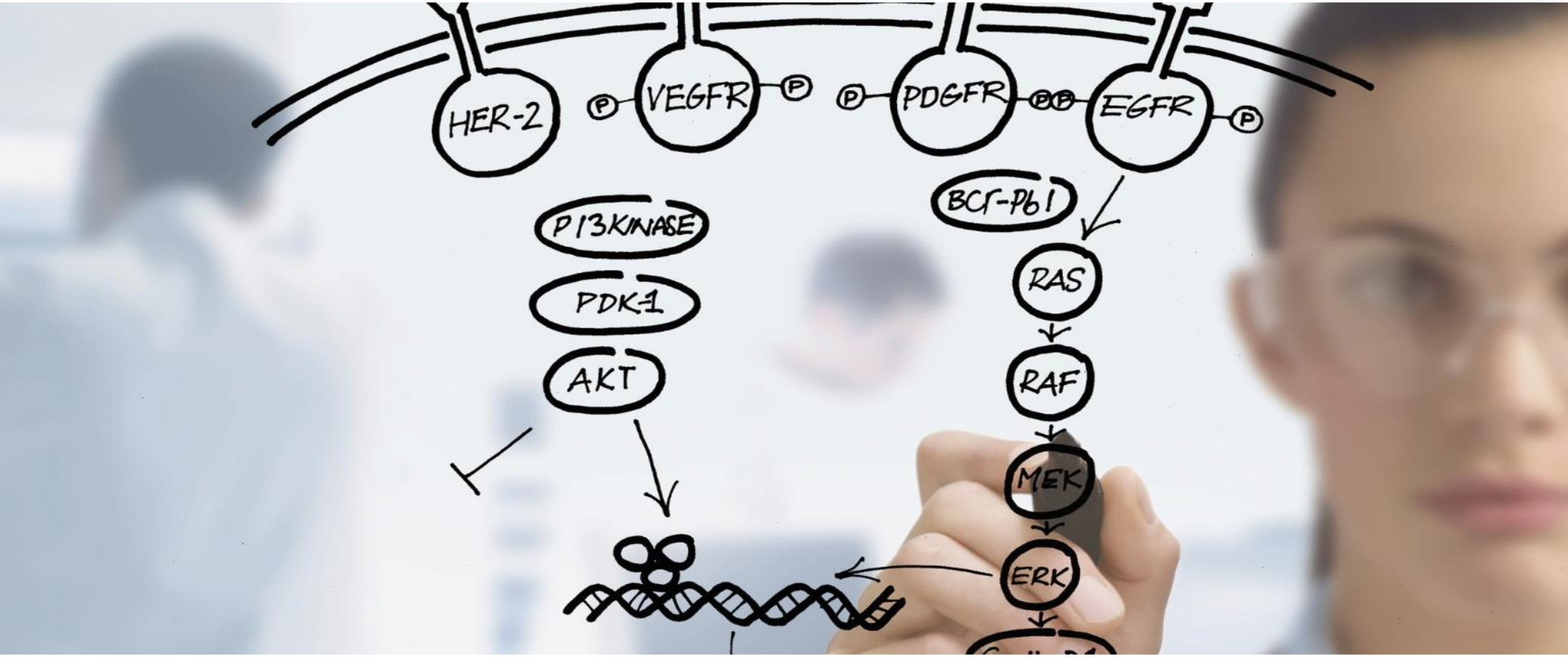
- All entities:
  p-value < 0.05
- Diseases、Functions、
  Upstream regulators:
  z-score≧2
- All molecules types
  (except chemicals)

- Activated nodes
  z-score≧2
- Inhibited nodes
  z-score≦-2

Content-based machine learning



This also applies to inferred **molecule-function relationships**, but in this case the predicted relationships can also be interpreted as being **causal**.



歡迎與我們聯絡

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